Message

From: Cogliano, Vincent [/O=EXCHANGELABS/OU=EXCHANGE ADMINISTRATIVE GROUP (FYDIBOHF23SPDLT)/CN=RECIPIENTS/CN=51F2736376AC4D32BAD2FE7CFEF2886B-COGLIANO, VINCENT]
Sent: 1/18/2011 8:23:55 PM
To: Everhart, Cheryl (ATSDR/OA/OD) [bqf5@cdc.gov]
Subject: Re: Request for Conference call Dr. Christopher Portier

Hello Cheryl -- I was out all morning, but 4:30 today (Tuesday) would be fine if it still fits Chris's schedule. My office number is below ... Best regards, Vince

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From: "Everhart, Cheryl (ATSDR/OA/OD)" <bqf5@cdc.gov>
To: Vincent Cogliano/DC/USEPA/US@EPA
Date: 01/17/2011 06:07 PM
Subject: Request for Conference call Dr. Christopher Portier

Dr. Cogliano,

Dr. Christopher Portier, Director, National Center for Environmental Health/Agency for Toxic Substances and Disease Registry/CDC, would like to schedule a 30 minute conference call with you for Tuesday, January 18, 2011, regarding EPA's Peer Review: IRIS Toxicological Review of Hexavalent Chromium.

Dr. Portier is available at the following times:

12:00-12:30pm
12:30pm – 1:00pm
4:30pm-5:00pm

Would you be available for any of the above times? If so, please provide a number that Dr. Portier can reach you.

Should you have any questions, please let me know.

Thank you in advance for your assistance in this matter.

Cheryl Everhart
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Data Questions
EPA'S IRIS Assessments
(GAO Job Code: 361203)
Sent to EPA Monday, May 23, 2011

1) Is the "Actual Key Dates" spreadsheet a living document, or is it updated regularly?

   Response: Updated regularly.

2) Why do the Start Dates provided not match those previously agreed to by GAO and EPA?

   Response: The start dates in the August 3, 2010, and the May 6, 2011, tables appear to match. GAO will provide a list of start dates that do not match.

3) For the 31 chemicals listed on Document 4, there are no dates post-May 2009. The status of each is highlighted in gray in the document (e.g., Steps 1-4).

   a) Why are there not post-May 2009 Start Dates (drafting step) for these 31 chemicals?
   Response: There are "pick up dates" for chemicals that moved from Table 2 to Table 1. Other assessments passed no milestones after May 2009. See response to #3e.

   b) For those chemicals further along in the process, why are there not post-May 2009 dates for when the relevant steps began?

   c) **Response:** See response to #3e.

   d) Uranium and Copper are listed in the Current Status data as being in Step 3 (Interagency Review), but there are no new process dates for these assessments prior to this step and no new process start date for this step. Have these already begun the interagency review step, and if so, what is the review initiation date?

      Response: Uranium began interagency review on May 4, 2009. Copper began interagency review on February 4, 2008. Information on individual assessments is provided under 3e.

      i) How were these assessments "cut" at this step? **Response:** Unclear what this means.

      ii) Did negotiations with the interagency group take place to make these determinations?
      Response: EPA did not negotiate with the interagency group on any determinations as to how to proceed through the process with these assessments. The interagency group provided scientific comments, and EPA discussed the comments with the reviewers. Both assessments (copper and uranium) have difficult scientific issues that EPA has been working to resolve. In both cases, resolution of the issues will lead to a new assessment, which EPA intends to take through the review process again. More information is provided below in the response to 3e.

   e) Same questions for Chloroform & MTBE (Step 2 – Agency Review), DCB-1-2,3,4 & Platinum & Ethylene Oxide & Tetrahydrofuran & PERC (Steps 4 & 5)?

      Response: See #3e for responses to a & b. Question c doesn't apply because these assessments are not currently in interagency review.

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f) We need the post-May 2009 Start Dates and relevant step dates for all 31 of these assessments. Not all we have post May 2009 start dates. The discussion below provides these dates where there was an actual start or pick up after May 2009. Some assessment, like the phthalates started before May 2009 and work has been continuous with no breaks.

Response: It's not clear what is meant in the question by post-May 2009 start dates. EPA has provided post-May 21, 2009, "pick-up" dates for Table 2 chemicals that were moved to Table 1 as described below.

Since the current IRIS process went into place on May 21, 2009, NCEA has been working to reduce a backlog of assessments that have been under development and to complete assessments that are of high priority to EPA Program Offices or Regions. Throughout the past two years, the IRIS process has been evolving, and various tasks and work products have been added to the process, increasing the level of effort for each assessment and the amount of management review time. NCEA has consulted with agency and interagency reviewers on how to improve the process and has committed to additional activities to increase transparency and make the reviews more efficient for the agency and interagency reviewers. As a result, NCEA has found it necessary to revisit priorities and reassign staff to ensure that the highest priorities are being met. In addition, some assessments have been delayed because of issues that must be resolved at higher levels in EPA. The list below provides the requested information for each of the 31 chemicals.

In the terminology used below, Table 1 and Table 2 refer to categorizations of IRIS assessments that were made in 2008 when NCEA decided to focus its resources on assessments in agency review or beyond and on a few other high priority assessments (Table 1 assessments). Table 2 assessments were assessments still in draft development. Staff members were reassigned to work on Table 1 chemicals. However, staff continued to put a lower level of effort into Table 2 chemicals when they had time. In November 2010, after several Table 1 assessments had been completed, some of the Table 2 assessments were fully staffed and moved to Table 1. The pick-up date refers to the date when the assessment was fully staffed and moving forward with a schedule reflecting the May 21, 2009, process.

- Ammonia should have a pickup date of 11/17/10. This is the date that it was staffed and moved from Table 2 to Table 1.
- Arsenic (inorganic) noncancer. This assessment went to Agency Review (step 2) along with the arsenic cancer assessment in 2005. The EPA Office of Water, which is the lead office on the IRIS arsenic assessment, decided that the cancer assessment was of higher priority and put the noncancer part of the assessment on hold while moving forward with the cancer assessment. The Office of Water has now taken up the noncancer assessment and is working on a draft for Agency Review. Since the draft has been substantially revised, the assessment will go through the complete process again. The pick- up date is May 12, 2009, when a task order was put into place.
- The peer review meeting for beryllium was held on July 16, 2008. The peer reviewers suggested a number of quantitative approaches to improving the inhalation unit risk (IUR) estimate. NCEA investigated these approaches but found that none could be implemented because of limitations in the epidemiological data and analyses available to EPA at the time. Throughout the development and review of the beryllium assessment, EPA has been

discussing with NIOSH a reanalysis of a NIOSH epidemiology study of beryllium and cancer that would support EPA's development of an IUR. In March 2010, NIOSH produced a new analysis of an occupational cohort exposed to beryllium that supports development of an IUR. Based on this analysis, NCEA is revising the beryllium assessment. Because the assessment will be completely revised and is essentially a new draft, NCEA intends to repeat the entire review process including a new external peer review and public comment period. The pick-up date is March 1, 2010, when the NIOSH study became available to EPA.

- Biphenyl should have a pickup date of 11/17/10. This is the date that it was staffed and moved from Table 2 to Table 1.
- t-Butanol should have a pickup date of 11/17/10. This is the date that it was staffed and moved from Table 2 to Table 1.
- Butyl benzyl phthalate is one of six phthalate esters that are part of EPA's cumulative phthalate assessment. Draft development for this complex assessment is taking longer than the standard period of less than one year. The start date is 3/31/09. There is no pick-up date after May 21, 2009.
- Cadmium should have a pickup date of 11/17/10. This is the date that the assessment was staffed and moved from Table 2 to Table 1.
- The chloroform assessment was originally led by EPA's Office of Water. The IRIS oral chloroform assessment, which was a higher priority for the Office of Water than the inhalation assessment, was completed in 2001. The inhalation assessment was eventually transferred to NCEA as the lead in 2007. NCEA expanded the assessment to include both the inhalation assessment and a reassessment of the oral assessment. The assessment has been through two rounds of Agency Review, with the last round occurring in September 2008. Since that time, complex issues related to the chloroform mechanism of action by both the oral and inhalation pathways have arisen. Only a limited number of NCEA staff that have the expertise to address the scientific issues. These staff members have been working on completing assessments including tetrachloroethylene and trichloroethylene, and we have been unable to resolve the issues without their input. We have recently staffed this assessment with a mode of action expert and are aiming for a release to agency review in July or August. The start date is 1/8/07. There is no pick-up date after May 21, 2009.
- The copper assessment began interagency review under the April 2008 process and transitioned into the 2009 process but has not completed interagency review. It is one of 2 transitional assessments of a total of 16, that have not moved forward from interagency review (7 have been completed – 1,1,2,2-tetrachloroethane, chloroprene, hydrogen cyanide, cis-1,2-dichloroethylene, trans-1,2-dichloroethylene, thallium, bromobenzene; 4 are scheduled for completion in FY11 -- inorganic arsenic cancer assessment, hexachloroethane, trichloroacetic acid, mirex; and 3 are moving forward after the agency removed the hold on assessments that used Ramazzini Institute data -- acrylonitrile, noncancer methanol assessment, and ETBE. The copper assessment has complex issues related to the fact that copper is an essential mineral that exhibits toxicity at levels close to the recommended daily allowance. This assessment has been delayed because EPA does not have a standard method for developing a quantitative assessment for essential minerals. NCEA is working with an outside expert to develop a method and a quantitative assessment for copper. When

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completed, the copper assessment will be a new assessment, and NCEA intends to send it back though the entire review process. The pick-up date for copper is 5/25/11.

- DEHP is one of 6 phthalates that are part of EPA's cumulative phthalate assessment. Draft development for this complex assessment is taking longer than the standard period of less than one year. The start date is 3/31/09. There is no pick-up date after May 21, 2009.
- DBP is one of 6 phthalates that is part of EPA's cumulative phthalate assessment. Draft development for this complex assessment is taking longer than the standard period of less than one year. The start date is 3/31/09. There is no pick-up date after May 21, 2009.
- The assessment for dichlorobenzenes has complex issues that only a limited number of staff can address. Staff members have been working on completing assessments including tetrachloroethylene and trichloroethylene, and we have been unable to resolve these issues without their involvement. We have recently staffed this assessment and are aiming for a release to final Agency Review in Fall 2011. There are no start or pick up dates after May 21, 2009.
- DIBP is one of 6 phthalates that is part of EPA's cumulative phthalate assessment. Draft development for this complex assessment is taking longer than the standard period of less than one year. The start date is 3/31/09.
- DINP is one of 6 phthalates that is part of EPA's cumulative phthalate assessment. Draft development for this complex assessment is taking longer than the standard period of less than one year. The start date is 3/31/09.
- DPP is one of 6 phthalates that is part of EPA's cumulative phthalate assessment. Draft development for this complex assessment is taking longer than the standard period of less than one year. The start date is 3/31/09.
- ETBE completed external peer review in March 2010. Shortly after the peer review meeting, the National Toxicology Program informed EPA that an analysis of leukemias identified in a cancer bioassay conducted by the Ramazzini Foundation raised concerns about the data from that laboratory. Subsequently, EPA placed a hold on six IRIS assessments including ETBE that relied on Ramazzini Foundation data. Also in March 2010, the Japanese Petroleum Energy Center published a two-year bioassay that provided data that could support both cancer and noncancer quantitative assessments for ETBE. On April 11, 2011, EPA removed the hold on ETBE and announced to the public that EPA would not rely on Ramazzini data for the quantitative analysis. Consequently, EPA is analyzing the JPEC data and developing a new assessment. Because this will be a new assessment, the assessment will go through the complete review process including a new external peer review and public comment period. The new start date is 4/11/11. NOTE: Date of EPA press release announcing removal of hold.
- The ethylene oxide assessment was delayed because staff and management resources were diverted to other assessments including formaldehyde, trichloroethylene, and tetrachloroethylene. There is no start date after May 2009.
- Hexabromocyclododecane should have a pickup date of 11/17/10. This is the date that it was staffed and moved from Table 2 to Table 1.

- Hexachlorobutadiene should have a pickup date of 11/17/10. This is the date that it was staffed and moved from Table 2 to Table 1.
- The MTBE assessment has been through two rounds of agency review. The assessment was placed on hold because it relies on data from the Ramazzini Instiute. The new pickup date is 4/11/11.
- Nickel should have a pickup date of 11/17/10. This is the date that it was staffed and moved from Table 2 to Table 1.
- The platinum assessment was delayed because of concerns raised by the halogenated platinum industry that were addressed at higher levels in EPA. There are no milestone dates after May 21, 2009. The assessment is moving forward and is scheduled to go to interagency science discussion and final Agency Review in August 2011.
- Tetrachloroethylene was reviewed by the National Academy of Sciences. The peer review report was published in February 2010. Since that time, EPA has been revising the report to respond to the peer review comments. This is a major assessment with significant comments. Responses required extra time to develop. There is no milestone date after May 2009. Tetrachloroethylene is currently in the final Agency Review and interagency science discussion and is scheduled for completion in September 2011.
- The tetrahydrofuran assessment was originally led by EPA's Office of Pollution Prevention and Toxics. This assessment has complex issues that only a limited number of staff can address. Staff members have been working on completing assessments including tetrachloroethylene and trichloroethylene. We have recently staffed this assessment with a mode of action expert and are aiming for a release to final Agency Review and interagency science discussion in July 2011.
- 1,2,4- and 1,3,5-Trimethylbenzene should have pickup dates of 11/17/10. This is the date that these assessments were staffed and moved from Table 2 to Table 1.
- Uranium. Uranium began interagency review under the April 2008 process and transitioned into the 2009 process but has not completed interagency review. It is one of the two transitional assessment, of a total of 16, that has not moved forward (7 have been completed; 4 are scheduled for completion in FY11; and 3 are moving forward after the agency removed the hold on assessments using Ramazzini Institute data). This assessment has complex issues related to the fact that the RfD developed in the Agency and interagency review drafts was at or below background levels. The database was reevaluated based on comments received and a new RfD based on a different endpoint was developed. Since the assessment is essentially new it will go through the complete process again starting with a full Agency Review. There is no start date after May 2009.

4) For Cumulative Phthalates, why is there no Start Date listed?

Response: This is an oversight. The start date is 3/31/09.

5) The data shows Mirex entering the 2nd simultaneous interagency/EPA reviews on 4/8/2010 and holding an interagency meeting on 5/25/2010, but the Current Status data you recently sent shows Mirex in Step 4 (External Peer Review). According to recent correspondence, "EPA incorporated additional modeling efforts post peer review as a result we decided to conduct a letter peer review of some new modeling in the mirex assessment. The EPA Contractor is

assembling a group of reviewers. Assuming the review is favorable, the assessment will be posted in FY11." Will Mirex go through an additional simultaneous interagency/EPA review?
Response: NOTE: Not sure about this. I believe we said yes at the meeting.

a - Had the 2nd round of interagency/EPA reviews been completed before this additional peer review was initiated?

Response: Yes

b - The assessment appears to have been completed last summer, why did it not post before the recent desire for additional peer review?

Response: After the agency and interagency reviews are completed, the assessments go through a clearance procedure that involves briefings of NCEA and ORD management. Upon hearing of the significant changes that were made in the assessment in response to the peer review, the EPA management decided that another peer review was warranted.

i) Why did the new modeling go to peer review?

Response: It was decided that the changes were significant enough to warrant an additional peer review.

ii) When and by whom was the decision made to initiate the additional peer review?
Response: This decision was made at the ORD Assistant Administrator level.

6) Has ETBE restarted completely?

Response: See response to #3e.

7) Please explain the Arsenic and ETBE dates.

Response: See response to #3e.

8) For Naphthalene, why is the Start Date listed more recent than the Nov. Table 1 pick-up date?

NOTE: I don't know where the naphthalene start of 2-11-11 came from. The pick-up date is November 17, 2010.

9) For Urea, why did both Step 2 and Step 3 take so long?

Response: This was a Table 2 chemical that NCEA moved to Table 1 because it is a fairly simple assessment that would likely move quickly. It was delayed because management review focus was on other higher priority assessments we were trying to get out in that time frame such as formaldehyde and trichloroethylene.

10) For numerous chemicals, why did date values change from the initial source to the more recent updates?

Response: The table has been rechecked and an updated, corrected table has been provided.

11) For Trichloroacetic Acid, why does the Step 3 date of 8/18/09 have a question mark by it?

Response: The comment due date has been removed. EPA did not solicit comments for transitional chemicals such as trichloroacetic acid, because comments had already been received under the earlier interagency review process.

12) For Hydrogen Cyanide and Tetrahydrofuran, why are the Start Dates listed as 2002 and 2003, respectively, without greater precision?

Response: When we don't have a precise start date, we use the date the assessment first appeared on the agenda.

13) For Dioxin, why are all of the Step 2 and Step 3 dates identical?

Response: Dioxin wasn't in the IRIS process until it when to external peer review. Before that it had its own process that did not completely correspond to the steps in the IRIS process.

14) For Chlordecone, why is the date listed for the Step 3 interagency meeting identical to the Step 6B interagency meeting (despite the surrounding dates being years older)?

Response: This is a typographical error which has been corrected.

15) For 1,4-Dioxane (oral), the Listening Session date was announced in the FR Notice as 07/06/09. This was the date given in the first version of the Actual Key Dates table. Recent versions list the Listening Session as 6/24/09.

Response: The correct date for the listening session is 7/6/09.

16) For 1,2- and 1,3-DCB, why are the Start Dates for Step 4 listed as being in 2004 when all surrounding dates are 2005 and 2006?

Response: These assessments were started in 2002 under a different IRIS process referred to as the consensus review process in which the external peer review preceded the agency review. The process was changed in early 2003-04 for new assessments so that external review followed agency review, but older assessments continued to follow the consensus review process. Interagency review was phased in to the process on an informal basis starting around 2005.

The actual schedule is:
Release of assessments for peer review and public comment – Jan. 30, 2004
Peer review meeting – Feb. 12, 2004
End of public comment period – March 1, 2004
Begin agency consensus review – June 9, 2004
Begin interagency review – September 30, 2005
At this point, a new inhalation cancer assessment for 1,4-DCB had been incorporated based on new data. EPA decided to send the assessment to a focused peer review. The remaining schedule is for 1,4-DCB only.
Begin focused external peer review – July 11, 2006
End public comment period – October 17, 2006
Peer review meeting – November 3, 2006

17) For Copper, why is the Step 3 Start Date of 2/4/08 listed as the comment due date in the initial data source (footnote specifies Step 3 began 12/21/07)?
Response: [NOTE: Stan –The Margolies excel file gives a date of 12/21/07 for start of interagency review. 2/4-08 is indicated as the date the comments were received. I believe you changed the start of IAR to 2-4-08. Please check this.]

18 - We do not have Start Dates under the old process for n-Butanol, Diethyl phthalate, and PCBs (noncancer), but they first appeared on the IRIS Agenda in 2008, 2008, and 1998, respectively. What work was done on these 3 chemicals prior to May 2009 (e.g., lit searches, drafting, etc.)?

Response: The literature search for n-butanol was completed in October 2007. At that time no chemical manager had been assigned. The IRIS process at that time was to have a contractor conduct literature searches on all the FY2008 new starts and use the results to assign chemical managers and decide which assessments start first. A chemical manager was assigned in 2009, and the contractor work assignment for draft development went into place on 2/11/09. Chapters 1-4 were delivered 11/9/09. Limited work proceeded on PBPK modeling while the chemical manager was reassigned to Table 1 chemicals. n-Butanol was moved to Table 1 on 11/17/10 and entered Agency Review May 6, 2011.

The literature search for diethyl phthalate was also completed in October 2007. Chapters 1-4 of the Toxicological Review were drafted by a contractor and delivered to EPA in December 2007. No additional work was done until FY11.

19) Why are relevant drafts and comments not posted online for Asbestos (Libby), ETBE, Bromobenzene, Chloroprene, Hydrogen Cyanide, Tetrachlorothane, Thallium, Mirex, and Acrylonitrile?

Response: Only interagency comments received after May 21, 2009, are posted on the IRIS web site and on regulations.gov. Interagency drafts and comments are posted when the assessment is released for public comment (step 3 comments) and when the assessment is posted as final (step 6 comments). The Libby assessment has not yet been released to the public, so no comments are posted. Mirex comments will not be posted until the assessment is released as final. The acrylonitrile assessment had not been released when this question was submitted. The acrylonitrile assessment was released June 30, 2011, and interagency comments received after May 21, 2009, have been posted. The other assessments are all transitional assessments that were in interagency review on May 21, 2009. EPA received no interagency comments on any of these assessments after May 21, 2009.

20) How do you post drafts and comments online (separately) for Step 3 and Step 6B?
Response: NCEA posts interagency comments online when the draft is released for public comment (step 3 comments) and when the draft is becomes final (step 6 comments). Step 3 draft and comments are posted on the NCEA/IRIS website and on the federal docket (www.regultions.gov). The purpose of posting on the federal docket is to have a repository for the public to submit comments electronically where the comments can be viewed. The Step 6 comments are posted only on the NCEA/IRIS website.

What is the reasoning behind this posting approach?

Response: The IRIS process calls for the interagency comments to be made part of the public record. The reason for posting the comments is to increase the transparency of the IRIS process for the public.

How do you ensure that drafts and comments will remain accessible to the public?

Response: The comments are retained on the IRIS database under Recent Additions. NCEA is currently making revisions to the IRIS database that will allow users to access the interagency drafts and comments directly from the IRIS summary.

When are drafts and comments posted online (e.g., immediately when they are submitted by interagency reviewers, when drafts go to external peer review, when staff is available, etc.)?

Response: With rare exceptions, Step 3 draft and comments are posted on the IRIS website and on the federal docket the same day that the external review draft is released for public comment. Posting on the federal docket may lag a day or two depending on the workload of the EPA docket staff. The Step 6 draft and comments are posted on the IRIS website (but not on the docket) on the day the document is published or shortly after.

TESTIMONY OF

Rena Steinzor
Professor, University of Maryland School of Law
and
President, Center for Progressive Reform (www.progressivereform.org)

before the

U.S. House of Representatives

Committee on Science, Space, and Technology,
Subcommittee on Investigations and Oversight

EPA's IRIS Program:
Evaluating the Science and Process behind Chemical Risk Assessment

July 14, 2011
Washington, D.C.

Mr. Chairman, Ranking Member Edwards, and members of the Subcommittee, I appreciate the opportunity to testify before you today on one of the Environmental Protection Agency's (EPA) most important and foundational programs, the Integrated Risk Information System (IRIS). Let me get straight to the point. These days, the more important a public health program, the more likely it is to be the subject of relentless, intemperate, and unjustified attacks. IRIS is no exception. What is in fact a sober, well-informed, and carefully conducted scientific effort to synthesize existing research in order to set reference doses for the most toxic chemicals is portrayed by industry lobbyists as an anti-scientific effort to "demonize" such ostensibly benign substances as arsenic, formaldehyde, and dioxin. This deliberate misreading of the science by industry lobbyists is intended to prolong Americans' exposure to dangerous substances in the service of corporate profit, while at the same time immobilizing the federal agency best qualified to protect public health, the EPA.

The truth is that everyone attending this hearing would be hard-pressed to come up with more than a dozen examples of toxic chemicals that have been found to be significantly less harmful than we originally thought when additional research was done. The powerful historic trend moves strongly in the opposite direction: as the research has accumulated, chemicals like dioxin, arsenic, formaldehyde, cadmium, mercury, and lead prove to be *more* toxic than we first imagined. Endless efforts to deconstruct individual studies should not obscure this trend, as the chemical industry was well aware until the current backlash against regulation offered it new opportunities to defeat safeguards that protect public health by distorting EPA's track record.

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IRIS started as an internal EPA database used to develop toxicological profiles for common chemicals. These profiles set the reference dose, or RfD, for a given chemical on the basis of existing scientific literature. An RfD is the amount below which human exposure is deemed unlikely to cause adverse health effects. Over time, IRIS has become an invaluable resource: It receives some 2,000 internet visits a day, testament to its importance as among the best, most comprehensive databases for this kind of baseline information. And, although IRIS itself most definitely is *not* a regulatory program, it provides a strong scientific foundation for much of the rest of the agency's work. Without the scientific determinations IRIS contains, EPA would be hard-pressed to develop standards for the control of emissions of toxic chemicals that cause brain damage, cardiovascular illness, reproductive dysfunction, cancer, and a range of other diseases. Delaying the production of IRIS profiles costs lives and endangers public health, an intolerable outcome that this Committee must not allow to happen.

My testimony today makes four points about the future of the IRIS program:

- ***From the American public's perspective, the central and urgent problem with IRIS is not that it rushes to judgment on toxic chemicals. Far from it. The problem is that repeated rounds of redundant "peer review" and interagency comment allow – in fact, invite –chemical manufacturers, the Department of Defense, and other self-interested parties to slow the program to a crawl.*** Because these delays help to ensure that dangerous chemicals are left in commerce for years longer than necessary, people suffer avoidable diseases and irrevocable neurological and reproductive damage. The Government Accountability Office (GAO) has repeatedly warned Congress about the negative implications of these delays. See, e.g., GAO-08-6743T, EPA's New Assessment Process Will Increase Challenges EPA Faces in Evaluating and Regulating Chemicals (April 29, 2008) and GAO-09-271, HIGH-RISK SERIES, An Update (January 2009). GAO has placed the EPA chemicals program in the "high risk" category reserved for a small number of the most troubled programs in government. It made this important decision in part because IRIS updates are so slow that the data base risks becoming obsolete. It did not make any reference to the distorted critique of EPA science that the chemical industry has developed.

- ***Given that IRIS is constantly struggling to avoid capture by the chemical industry and, if anything, gives manufacturers far too many opportunities to befuddle final assessments, the chemical industry's sudden discovery of its flaws is as opportunistic as it is incredible.***

- ***The National Research Council's (NRC) report on formaldehyde does not justify the radical changes sought by the industry. In fact, the NRC explicitly endorsed the program's continuation and improvement.*** Its critique of the formaldehyde assessment constitutes robust peer review, not an outright condemnation of the program and EPA science as industry witnesses would have you believe. I wish that the NRC committee had not adopted such a haughty tone in scolding EPA staff. But that tone was the product of political naiveté regarding how its report would be exploited in the existing political climate. It cannot fairly be characterized as a recommendation that IRIS stop—or even slow—its critical work.

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- ***The remedies sought by the American Chemistry Council (ACC) are designed to run IRIS off the road, further undermining EPA's mission to protect public health. I urge the Committee to side with the public, not the manufacturers of toxic chemicals long overdue for assessment and control.***

I am a law professor at the University of Maryland School of Law and the President of the Center for Progressive Reform (CPR) (http://www.progressivereform.org/). Founded in 2002, CPR is a 501(c)(3) nonprofit research and educational organization comprising a network of sixty scholars across the nation who are dedicated to protecting health, safety, and the environment through analysis and commentary. I joined academia mid-career, after seven years as an attorney at the Federal Trade Commission, five years as staff counsel to the House Energy and Commerce Committee, and seven years representing small and mid-sized electric utilities. My work on environmental regulation includes four books, and over twenty-seven articles (as author or co-author). My most recent book, published by the University of Chicago Press, is *The People's Agents and the Battle to Protect the American Public: Special Interests, Government, and Threats to Health, Safety, and the Environment*, which I co-authored with Professor Sidney Shapiro of Wake Forest University's School of Law, analyzes the state of the regulatory system that protects public health, worker and consumer safety, and natural resources, concluding that these agencies are under-funded, lack adequate legal authority, and are undermined by political pressure motivated by special interests. I have served as a consultant to EPA and have testified previously before Congress on regulatory subjects on numerous occasions.

Saving IRIS

Since 2005, Member Scholars at the Center for Progressive Reform (CPR) have researched and written five white papers regarding IRIS and the need to streamline the process for developing toxicological profiles and several letters to decision makers concerned about the program's future. They are available here: http://www.progressivereform.org/IRIS.cfm, and I have attached the two most recent reports, *Corrective Lenses for IRIS* and *Setting Priorities for IRIS* to this testimony. Our key findings include:

1. IRIS is woefully incomplete. EPA is many years behind in completing profiles of at least 255 chemicals. Some 109 chemical profiles that EPA was required by the Clean Air Act Amendments of 1990 to have completed by 2008 are either included in IRIS but missing critical elements, or entirely absent from the database. A similarly sad situation afflicts the agency's efforts to carry out the statutory mandates of the Safe Drinking Water Act. Every five years, EPA generates a new Contaminant Candidate List (CCL). The lists contain recommendations both for chemicals and microbiological contaminants. Since 1996, EPA has published three CCLs that contain 156 distinct chemical substances. IRIS profiles are missing for 64 (41 percent) of these substances.

2. So severe are the delays in the IRIS process that a 2008 GAO report warned that the Bush Administration's approach to IRIS, which resulted in just *two completed profiles per year*, left the database at risk of becoming obsolete. (The report is

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available at http://www.gao.gov/new.items/d08743t.pdf.) To its credit, the Obama Administration revised the IRIS process in an effort to speed the production of assessments, and has managed to increase the number of completed profiles to nine annually. But although this performance is a definite improvement, the rate of production is still slow enough that, if nothing else is done to improve the pace of IRIS, EPA will not catch up with its existing backlog for another *55 years*.

3. One area of particular concern is that the Obama Administration's new IRIS process left in place many of the roadblocks GAO had previously identified, including interagency review of individual assessments, multiple reviews by outside science panels, and prioritization of a few high-profile assessments at the expense of faster assessments. Potentially regulated parties, including other federal agencies like the Department of Defense and National Aeronautics and Space Administration, have targeted IRIS as a choke point for regulation. The labyrinthine process they have demanded, diagrammed on page 9 of the *Corrective Lenses* report, contains multiple rounds of peer review, public comment, and interagency review that are as redundant as they are time-consuming. In effect, the program suffers from the problem of "information capture"—a phenomenon where potentially regulated industries and their federal agency clients submit so much irrelevant data to EPA, and do so with such frequency, that new assessments become mired in never-ending controversy.

4. To close data gaps and reestablish IRIS's credibility as a cutting-edge database, EPA needs to make four changes. First, EPA should reduce the procedural burdens that were formalized during the Bush administration. Second, EPA must articulate clear, statute-driven priorities about which assessments to complete to ensure that data gaps in statutory mandates would be more quickly addressed. Third, the IRIS process must be restructured to allow for timely assessments to be written on the basis of the weight of available evidence at the time an assessment is undertaken. Fourth, EPA must have adequate resources—and use those resources efficiently--to complete a much larger number of assessments.

One additional point is worth making. The chemicals we are talking about here are the worst of the worst, produced in amounts of millions of pounds annually. As just one example, chromium compounds, which are categorized in the worst ten percent of all toxic chemicals and are among the hazardous air pollutants missing from IRIS, are emitted in amounts exceeding 58 million pounds annually. Unsafe exposure to chromium compounds causes cancer, suppresses immune systems, and harms kidney and respiratory functions. Over the last several years, industry has sponsored several studies of chromium. When a study documents adverse effects at common levels of exposure, the sponsors commission a second study designed to rip apart the first. Unfortunately, the victims of this endless treadmill are neither the sponsors, nor the scientists engaged in chasing each other's tails, but rather the public's health.

Industry Influence over IRIS

Anyone who has observed IRIS for many years cannot help but find the chemical industry's recent denunciations of the program disingenuous, even surreal. Far from being

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helpless bystanders in the process, industry members have been in the thick of the action since the database was initiated, submitting the research they think most important and repeatedly advocating their view of the research to IRIS staff, more senior EPA officials, sympathetic federal agencies and departments, and the White House Office of Information and Regulatory Affairs (OIRA). To whatever extent that IRIS science is flawed, the people complaining about those flaws are full partners in its development. In fact, one reason why IRIS profiles have ballooned into unmanageable length is the reaction of EPA staff to constant harassment by industry participants.

The Formaldehyde Review

The NRC conducted a robust peer review of the draft IRIS formaldehyde assessment. The report is written in the detailed language of one group of scientists giving another group of scientists an unvarnished assessment of how a scientific finding could be revised and bolstered. Its work will undoubtedly improve the IRIS process, and EPA is already taking its recommendations to heart.

Unfortunately, the NRC reviewers also succumbed to the fatal attraction of reiterating their professional superiority, using tough, even haughty language to critique EPA's work, and exhibiting a remarkable level of insensitivity to how their comments would be interpreted in the over-heated political atmosphere that afflicts the nation's Capitol these days. Clearly, the NRC committee was trying to help IRIS staff to do better, not to immobilize the program. Consider the following direct quotes from the NRC report:

> The draft IRIS assessment *correctly concludes* that formaldehyde is a genotoxic (DNA-reactive) chemical that causes cytogenetic effects, such as mutations. (emphasis added) (p. 4)

> The committee recognizes that revision of the approach will involve an extensive effort by EPA staff and others, and *it is not recommending that EPA delay the revision* of the formaldehyde assessment to implement a new approach. However, models for conducting IRIS assessments more effectively and efficiently are available, and the committee provides several examples in the present report. Thus, EPA might be able to make changes in its process relatively quickly by selecting and adapting existing approaches. (emphasis added) (p. 11)

As a person who teaches for a living, I would urge future NRC panels to keep in mind how much self-important scolding can interfere with a student's learning process—we all know that truth in our academic lives but may forget it when we enter the policymaking world. Regardless, Congress would make a grave error if, at the behest of self-interested chemical manufacturers, it ignored the stated goals of the NRC's review.

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Excessive Remedies

The remedies proposed by the chemical industry representatives here today confuse and distort the core purposes of IRIS. For example, one of the most intemperate proposals advanced by the American Chemistry Council is that the OIRA increase its oversight of the program. OIRA is the division within the White House that checks agency cost-benefit analyses. It is staffed almost exclusively by economists who have no better idea of what constitutes a good RfD than any other lay person. Two scientists work at OIRA, in comparison to the dozens of well-qualified scientists representing multiple disciplines who work at EPA. The recommendation that OIRA be put in charge of IRIS is not designed to improve the program's scientific validity, but rather is intended to give chemical manufacturers a sympathetic forum where they can tie IRIS in knots more easily.

A second industry demand voiced by ACC is that NRC be brought in to review *all* IRIS assessments. NRC is the gold standard for peer review and, as I mentioned earlier, its critiques are always interesting. On the other hand, the academic scientists who serve on NRC review committees receive compensation that does not nearly pay for their time. Instead, they are motivated by a commitment to public service, the pleasure of engaging with bright and sophisticated colleagues, and the prestige of serving by invitation on a panel convened by the finest scientific institution in the nation. Using NRC to run around double-checking government work would corrode this delicate balance, ultimately rendering it unworkable. Not incidentally, it would also add unreasonable delay to an already dangerously slow process. I hope that the NRC recognizes the insidious implications of this recommendation and strongly opposes it.

The invocation of NRC, and the National Academies as a whole, has become a common practice for potentially regulated parties who hope to slow down EPA decision making. The little-recognized hypocrisy of this practice is that when NRC ratifies EPA's judgments without qualification, aggrieved industry participants simply ignore its findings and proceed with their campaign against the agency. So, for example, NRC issued a report on mercury that was fully supportive of the RfD that EPA had set for the substance. (The NRC report is available at http://www.nap.edu/openbook.php?isbn=0309071402.) The electric utilities fighting EPA's regulatory efforts simply ignored the NRC report as if it had never been completed, continuing their attacks on the research underlying the agency's decision. Far from serving as an umpire in heated disputes, NRC was exploited as a tool to delay final action and then promptly cast aside.

The final, penultimate example of overreaction that will endanger public health is the rider now pending in the House Appropriations Committee. It would bar EPA from moving forward with future assessments until all existing assessments had been revised to conform to the NRC's advice about the formaldehyde assessment. This proposal would paralyze the IRIS program for the foreseeable future by forcing its staff to engage in a massive round of paper shuffling.

In a surprisingly successful effort to obscure the real motivations behind these radical suggestions, regulated industries have portrayed them as essential to job creation, and therefore of direct benefit to the average American. Fundamental to this set of claims is the notion that

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regulatory excesses in these times of economic recession have hit industry so hard that its members cannot afford to expand their businesses and put people back to work. But some quick research on the percentage increase in profits from 2009 to 2010 for some of the ACC's largest members yielded surprising results.

Company	Fortune 500 Rank	Increase in Profit 2009 to 2010
Dow	45	19.4%
Dupont	84	19.98%
PPG Industries	181	9.7%
Praxair	241	13.0%
Air Products & Chemicals	271	7.7%
Ashland	272	11.2%
Eastman Chemical	348	32.6%
Avery Dennison	356	9.4%
Celanese	388	16.5%
Lubrizol	423	18.1%

Source: CNN Money, Issue date: May 23, 2011,
http://money.cnn.com/magazines/fortune/fortune500/2011/industries/7/index.html

Rules to protect public health and the environment most definitely do not have the effect of sweeping money into a pile and setting it on fire. Rather, they save the lives of millions of people, prevent many more millions from getting sick or becoming sicker, and preserve the irreplaceable natural resources without which human life would be impossible.

For example, Clean Air Act regulations are uniformly recognized as a wonderful economic bargain by honest experts from all points on the political spectrum. According to EPA's very conservative numbers, which dramatically understate benefits and overstate costs, clean air rules saved 164,300 adult lives in 2010, and will save 237,000 lives annually by 2020. EPA estimates that the economic value of Clean Air Act regulatory controls will be $2 trillion annually by 2020; costs of compliance in that year will be $65 billion. Air pollution controls saved 13 million days of work loss and 3.2 million days of school loss in 2010. By 2020, they will save 17 million work loss days and 5.4 million school loss days. I emphasize that EPA's cost estimates are based on extraordinarily conservative assumptions regarding regulatory benefits. For example, EPA says that a non-fatal heart attack in a person 0-24 years old is worth only $84,000 and that an emergency room visit to treat an asthma attack is worth only $363 per incident—hospitals don't give you a plastic ID bracelet for that little.

And according to OIRA, which houses the staff of economists so embraced by ACC, "the estimated annual benefits of major federal regulations are in the aggregate between $132 billion and $655 billion, while the estimated annual costs are in the aggregate between $44 billion and $62 billion." (See
http://www.whitehouse.gov/sites/default/files/omb/inforeg/2011_cb/2011_cba_report.pdf.)

Thank you, Mr. Chairman and Ranking Member Edwards. I would be happy to answer any questions you may have.

Attachments:

1. *CPR Report, Corrective Lenses for IRIS*
2. *CPR Report, Setting Priorities for IRIS*

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Corrective Lenses for IRIS:

Additional Reforms to Improve EPA's Integrated Risk Information System

By CPR Member Scholars Rena Steinzor and Wendy Wagner and CPR Policy Analysts Lena Pons and Matthew Shudtz

CPR CENTER FOR PROGRESSIVE REFORM

Attachment 1

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CENTER FOR
PROGRESSIVE REFORM
WHITE PAPER #1009

October 2010

About the Center for Progressive Reform

Founded in 2002, the Center for Progressive Reform (CPR) is a 501(c)(3) nonprofit research and educational organization comprising a network of scholars across the nation dedicated to protecting health, safety, and the environment through analysis and commentary. CPR believes that sensible safeguards in these areas serve important shared values, including doing the best we can to prevent harm to people and the environment, distributing environmental harms and benefits fairly, and protecting the earth for future generations. CPR rejects the view that the economic efficiency of private markets should be the only value used to guide government action. Rather, CPR supports thoughtful government action and reform to advance the well-being of human life and the environment. Additionally, CPR believes that people play a crucial role in ensuring both private and public sector decisions that result in improved protection of consumers, public health and safety, and the environment. Accordingly, CPR supports ready public access to the courts, enhanced public participation, and improved public access to information. CPR is grateful to The John Merck Fund for funding this white paper, as well as to the Deer Creek Foundation, the Bauman Foundation, and the Open Society Institute for their generous support of its work in general.

This white paper is a collaborative effort of the following Member Scholars and Staff of the Center for Progressive Reform: **Rena Steinzor** is a Professor of Law at the University of Maryland School of Law, with a secondary appointment at the University of Maryland Medical School's Department of Epidemiology and Preventive Medicine, and the President of the Center for Progressive Reform; **Wendy Wagner** is the Joe A. Worsham Centennial Professor at the University of Texas School of Law, Austin Texas, and a Member Scholar of the Center for Progressive Reform. **Lena Pons** is a Policy Analyst and **Matthew Shudtz** is a Senior Policy Analyst with the Center for Progressive Reform.

For more information about the authors, see page 23.

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View of the Seattle Skyline through glasses courtesy of WikiCommons.

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Executive Summary

The Environmental Protection Agency's (EPA) Integrated Risk Information System (IRIS) is the most important toxicological database in the world. Not only is it the single most comprehensive database of human health information about toxic substances, it also serves as a gateway to regulation, as well as to a range of public and private sector efforts to protect against toxic substances. IRIS "profiles" of individual substances include a number of scientific assessments of the substance's toxicity to humans by various means of exposure – by inhalation, contact with the skin, and so on. Federal regulators rely on the assessments to do their important work protecting the public, as do state and local environmental protection authorities, and industry itself.

For EPA, the assessments conducted to complete profiles of particular toxic substances for IRIS provide the authoritative underpinnings for a wide range of regulatory actions under the Clean Air Act (CAA), the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA), and the Safe Drinking Water Act (SDWA). At the state and local level, IRIS profiles are the basis for regulation of toxic substances. For example, the Oregon Department of Environmental Quality used IRIS values in its Portland Air Toxics Assessment, conducted in 2006.[1] The Portland Air Toxics Assessment modeled ambient air concentrations of 12 pollutants at a highly localized level. Rather than having to rely on EPA's county-level assessment of toxic air pollutants, Oregon officials can now estimate exposure and risk at a neighborhood level and set permit allowances accordingly. In the private sector, IRIS information may be used in toxic tort suits, or by individuals or public interest groups to advocate for lower permissible permit levels under Title V of the CAA.

Unfortunately, IRIS is woefully incomplete. EPA is many years behind in meeting statutory mandates for completing profiles of at least 255 chemicals, and as a result regulatory and enforcement action related to those chemicals has been stalled. Some chemical profiles in IRIS are missing information essential to regulatory action. In addition, 77 of the hazardous air pollutants (HAPs) listed in IRIS are missing the most important piece of information – an assessment of how much of the substance may be safely inhaled. In all, some 109 chemical profiles that EPA was required by the Clean Air Act Amendments of 1990 to have completed by 2008 are either included in IRIS but missing critical elements, or entirely absent from the database. So severe is the delay in the IRIS process that a 2008 Government Accountability Office (GAO) report warned that the Bush Administration's approach to IRIS, which resulted in just two completed profiles per year, left the database at risk of becoming obsolete.[2]

In May 2009, newly appointed EPA Administrator Lisa Jackson introduced reforms she predicted would improve EPA's performance with respect to IRIS that included making it harder for other agencies of the federal government to slow down or exert undue influence over EPA's assessment of the environmental health effects of substances listed in IRIS. The Administrator's stated goal was to ensure completion of new assessments in 23 months, but she made no promises about how many assessments EPA would complete in a year. Neither

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did she present any plan for clearing the backlog of the 478 assessments that are in process, nor mention that EPA has long since been required by statute to complete, or have been identified as out of date by EPA staff.[3]

In the year since the new process has been in effect, EPA has made only modest progress completing assessments, finishing nine assessments in 2009 – up from the Bush pace of two per year – but still slow enough that, if it does nothing to improve its performance, EPA will not catch up with its backlog for another 55 years. Moreover, it is not clear from information available to the public whether the agency is fulfilling Jackson's 23-month pledge on individual IRIS assessments.

One area of particular concern is that the Administrator's new IRIS process left in place many of the roadblocks GAO had previously identified, including interagency review of individual assessments, multiple reviews by outside science panels, and prioritization of a few high-profile assessments at the expense of faster assessments.[4] The consequence is that significant data gaps are still a serious problem.

Specifically, the IRIS database is missing important human health information about the toxicological effects of HAPs, drinking water contaminants, and chemicals commonly found in Superfund toxic waste sites.

- **Thirty-two HAPs regulated under the CAA are not listed in IRIS at all, and 77 HAPs lack inhalation values, hampering the air office's ability to do the "residual risk assessments" that ensure technology-based standards provide an "ample margin of safety."[5]**

The Human Consequence of the IRIS Breakdown

The ramifications of the large-scale breakdown of the IRIS process are very real. For example, residents of the Marine Corps Base Camp Lejeune have been exposed to high levels of trichloroethylene for decades. A Navy-funded study of increased cancer risk for children born at Camp Lejeune found 14 cases of Acute Lymphocytic Leukemia in a cohort of 10,000-12,000 births, or more than 100 times the expected rate.

EPA drafted an updated IRIS assessment of trichloroethylene in 2001, but it was challenged by the Department of Defense (DOD). Under pressure from DOD, EPA commissioned a National Academy of Sciences Review of trichloroethylene. In 2007, five Senators introduced a bill instructing EPA to complete the trichloroethylene assessment and issue a drinking water standard for trichloroethylene. The bill was reported in the Senate, but has not passed in either chamber.

The Department of Defense objects to lowering the exposure limit for trichloroethylene because of the resulting increased cleanup costs. DOD estimates it would cost $5 billion more to clean up trichloroethylene if the drinking water standard went from five parts per billion to one part per billion.

Toward that end, DOD submitted 72 pages of comments to EPA's Nov. 2009 draft assessment of trichloroethylene. The new draft assessment will undergo review by the Science Advisory Board in 2010.

Meanwhile, EPA's IRIS assessment of trichloroethylene is still pending. Residents of Camp Lejeune continue to be exposed to high levels of trichloroethylene in drinking water, and cannot successfully prove these levels are harmful until EPA finishes this work.

— House of Representatives Committee on Science and Technology. Toxic Communities: How EPA's IRIS Program Fails the Public. (Jun. 12, 2008).

— Department of Defense. Comments on the Review of Trichloroethylene. (Aug. 25, 2009).

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- **Three of 71 contaminants regulated under the SDWA are not listed, and an additional 64 of 156 substances nominated to the Contaminant Candidate List, slowing EPA's ability to develop enforceable standards for drinking water contaminants.**
- **Of the 275 substances the Agency for Toxic Substances and Disease Registry has identified as "high profile" based on their frequency of occurrence at Superfund sites, toxicity, and potential for human exposure, 87 (32 percent) are not listed.**[6]

The sources of delay have not changed: priority treatment of complex, high-profile assessments at the expense of other needed assessments; excessive interagency review; involvement of the Office of Information and Regulatory Affairs (OIRA); industry interference; and recursive, formalized outside review continue to contribute to the small number of IRIS assessments completed each year.

The interagency review process is one of the largest sources of delay. It provides agencies, which are often also potentially regulated entities, with multiple opportunities to influence and soften EPA's risk assessments and reduce future regulatory burdens. Even under the new process, federal agencies, coordinated by OIRA, have two special opportunities to comment on draft IRIS assessments. EPA has the discretion to terminate the interagency review process, which is unusual and would not be tolerated at other agencies. The DOD, for example, would not allow EPA to comment on decisions about training because of concerns about hazardous pollution.

To close data gaps and reestablish IRIS's credibility as a cutting-edge database, EPA needs to make four changes. First, EPA should reduce the procedural burdens that were formalized during the Bush administration. Second, EPA must articulate clear, statute-driven priorities about which assessments to complete to ensure that data gaps in statutory mandates would be more quickly addressed. Third, the IRIS process must be restructured to allow for timely assessments made based on the weight-of-the-evidence at the time an assessment is undertaken. Fourth, EPA must also have adequate resources and make better use of its resources to complete a much larger number of assessments than it is currently finishing each year.

Administrator Jackson has repeatedly emphasized her commitment to use EPA's chemical management program to reinvigorate the agency's public health responsibility.[7] The IRIS program has featured prominently in her discussion of these efforts. EPA has substantial latitude to reforms the program and remove these obstacles to make it more productive. For Administrator Jackson to be successful with chemical management, she will need to impose further reforms on the IRIS process.

Tables 1 *and 2: Hundreds of millions of pounds of highly toxic chemicals are released each year without IRIS numbers that would allow EPA, state and local officials, the media, and community groups to gauge public health hazards.*

Table 1: Top Ten Hazardous Air Pollutants with No IRIS Information[1]

Chemical	Total Air Releases (lbs)
Chromium compounds	58,875,719
Ethylene oxide	19,326,422
Chloroprene	6,917,570
Diethanolamine	5,292,937
Ethyl acrylate	4,536,125
Cobalt compounds	4,502,987
Titanium tetrachloride	3,603,494
Cadmium compounds	1,736,020
O-Toluidine	626,844
Hydrogen fluoride	526,486
Total	**105,944,603**

Table 2: Top Ten Hazardous Air Pollutants with No Inhalation Values in IRIS[2]

Chemical	Total Air Releases (lbs)
Methanol	112,091,055
Carbonyl sulfide	353,389
Formaldehyde	313,659
Chlorine	270,468
Dichloromethane	205,328
Phenol	53,622
Trichloroethylene	48,130
Tetrachloroethylene	40,888
Lead compounds	14,478
Chloroform	12,191
Total	**113,413,298**

Figure 1,2 &3: *Hearing on Fixing EPA's Broken Integrated Risk Information System, Before the Subcomm. on Oversight and Investigations of the H. Comm. on Science and Technology* (Jun. 11, 2009).

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Introduction

The IRIS database provides a number of important pieces of information about the human health effects of specific toxic substances. These include specific oral and inhalation "reference doses," accounting for the effects of ingestion and inhalation of the substance, as well as a "cancer slope factor" that measures the risk of cancer associated with exposure to increasing concentrations of a substance. EPA relies on this information in developing regulations to protect Americans from a variety of risks, fulfilling its statutory mandate under several laws, including parts of the Clean Air Act (CAA), Safe Drinking Water Act (SWDA), Superfund and other statutes. IRIS is widely used, not just by EPA, but also by state, local, and international public health experts, as well as toxic tort attorneys. In all, the online version of IRIS receives approximately 20,000 hits per day.

Originally, IRIS was an internal EPA database, aggregating human health information collected by various offices within the agency. But the assessments grew to be so vital to the regulatory process and other risk-management decisions, that advocates for industry and the public interest began targeting IRIS assessments. In response, EPA has restructured the IRIS process three times since 2004. In doing so, EPA struggled to balance the need to complete IRIS assessments quickly with the desire to produce assessments that are so robust as to be immunized against criticism from outside interests.

EPA has failed to develop a process that can achieve this balance between providing information in a timely fashion so that the agency can get on with its work and attempting to generate definitive answers that demand a level of finality and precision that science cannot produce. The resulting IRIS assessment process has injected additional burdens, including interagency review coordinated by the White House Office of Information and Regulatory Affairs (OIRA) and recursive critique by outside scientists. These additional requirements slowed EPA productivity so significantly that although the IRIS program received increased funding from 2000 to 2007, the number of assessments completed in this period fell from an average of five per year to two per year.[8] After the Bush Administration's final round of reforms to the IRIS assessment process, congressional overseers estimated that it would take EPA six to eight years to clear all of the procedural hurdles between initiation of an assessment and its final posting in the public database.[9]

The Government Accountability Office (GAO) and the U.S. House of Representatives Committee on Science and Technology identified three primary problems with the Bush-era IRIS process: interagency review, multiple layers of science review, and EPA's choice to focus considerable resources on a few high profile assessments at the expense of progress on others.[10] In response, EPA Administrator Lisa Jackson announced a new IRIS process in May 2009. Jackson promised to regain control over interagency review and streamline each step so that assessments would be completed in 23 months. She explained that the new process would restore timely, transparent assessments in service of other actions to protect public health.[11] But Jackson's focus on completing assessments in 23 months rather than

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whittling down the prodigious backlog of uncompleted assessments suggests that it might be decades before the agency meets current statutory requirements whose deadlines have long since passed.

Indeed, the new IRIS process has failed to meet these goals precisely because it retained many of the same features of the old process. Interagency review of individual assessments, industry efforts to hijack the process through Data Quality Act petitions, overuse of science advisory boards, and a focus on high profile and complex assessments have all prevented EPA from completing assessments in a timely and transparent way. For example, under the new process, EPA releases written comments provided in the interagency review process, but the documents do not provide a full picture of what transpires between the agencies because they do not provide a record of telephone calls and other communications. And EPA's agenda for IRIS assessments has become less transparent, with less information available about which substances will be assessed and the projected timeline for doing so.

It might be decades before the agency meets current statutory requirements whose deadlines have long since passed.

With that in mind, this paper proposes five specific reforms to the IRIS process to make the program more productive and able to complete a greater number of assessments each year:

1. **EPA should adopt a transparent, statute-driven process for selecting substances to be assessed.**
2. **EPA should eliminate the interagency review process, which has largely served to create additional opportunities for industry interference, without adding significantly to the scientific discussion that should be at the heart of EPA's regulatory decision-making.**
3. **EPA should put faith in its own scientific expertise and rely on outside science review only in the most complex cases.**
4. **EPA Administrator Lisa Jackson should advocate for adequate resources for IRIS and ensure they are used to the greatest possible effect.**
5. **EPA should announce these reforms in a memorandum that also sets out a streamlined six-step process for developing an IRIS profile: (1) publish a notice of assessment in the Federal Register; (2) open a docket for public to add studies during staff literature review; (3) draft an assessment; (4) publish the draft for public and agency comment; (5) revise the draft based on input during the public comment process, and; (6) publish the final assessment to IRIS.**

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History of the EPA's IRIS Process

EPA has restructured the IRIS process three times since 2004. During the Bush administration, additional steps were added that provided OMB and other federal agencies a special opportunity to influence the process. EPA's current IRIS process eliminates some steps; however, some of the steps in the new IRIS process are not contained in the chart. Under the current process, OMB and federal agencies still have an opportunity to review IRIS assessments before the public comment period.

Figure 1: The original IRIS profile development process.

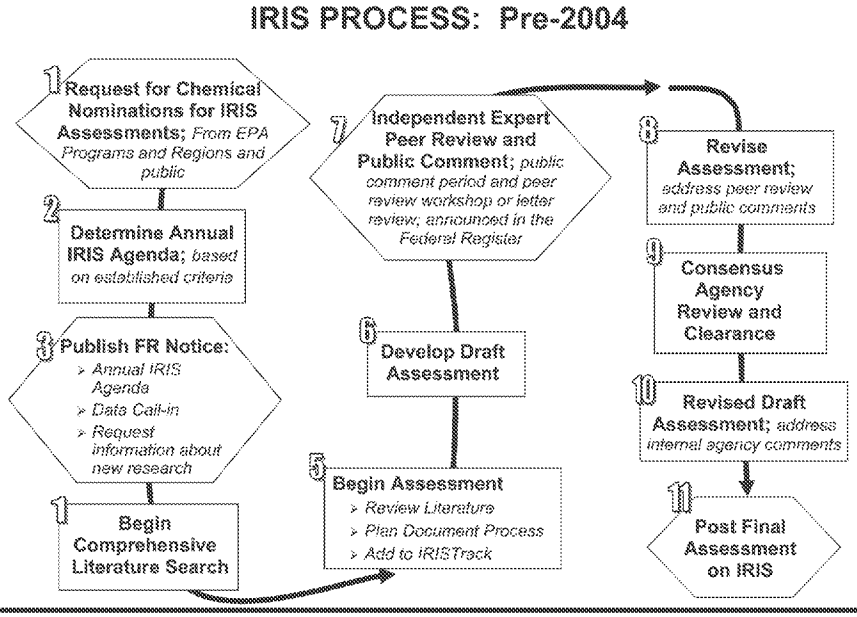
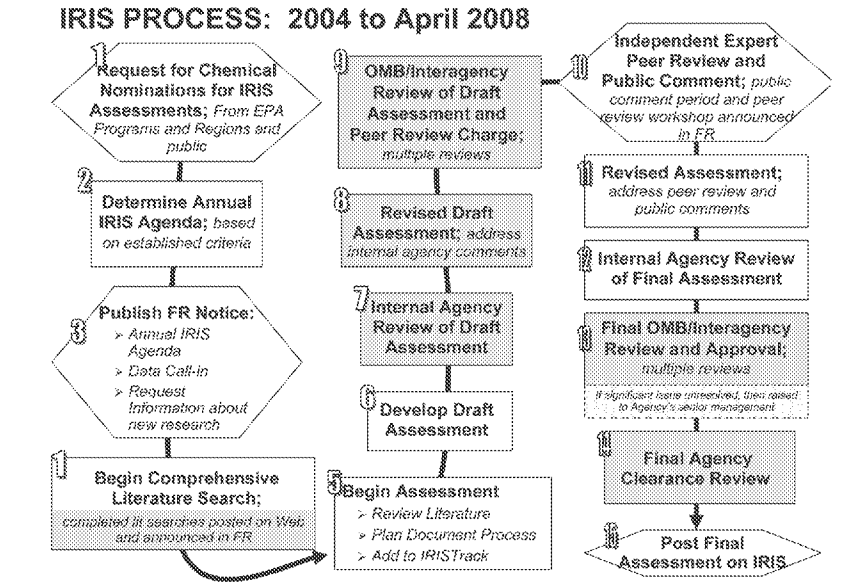


Figure 2: The process after the Bush Administration's first revisions.



Figures courtesy Environmental Protection Agency.

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Figure 3: The process after the Bush Administration's second revisions.

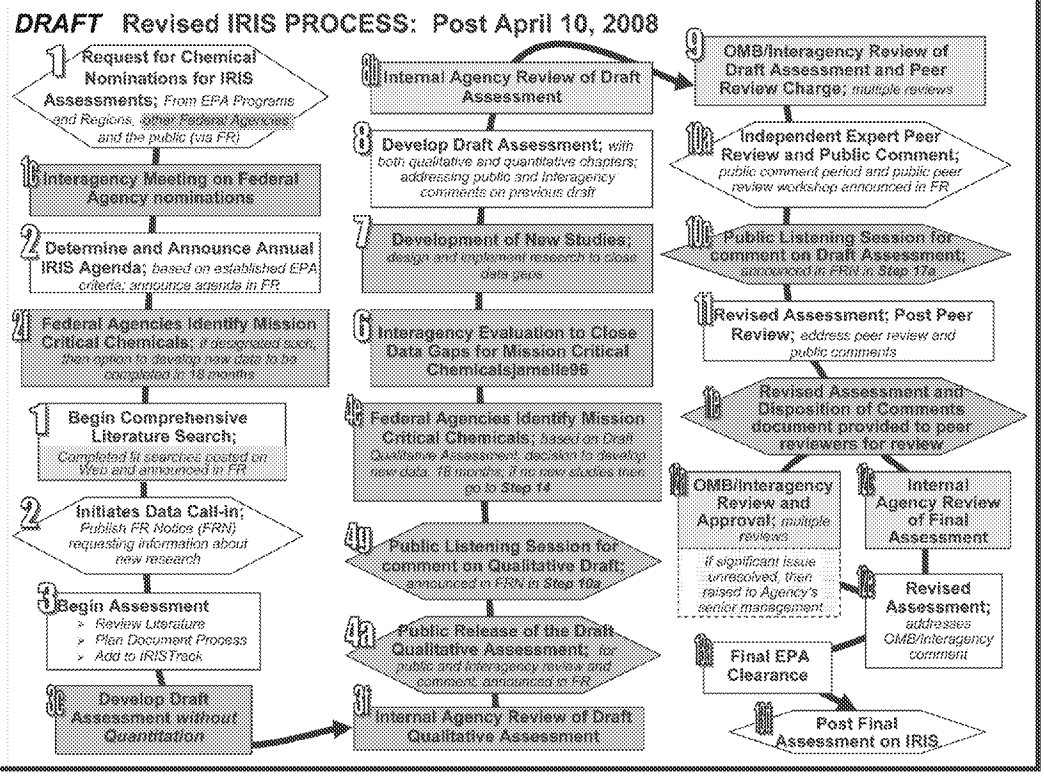

Figure 1,2, & 3: Hearing on Fixing EPA's Broken Integrated Risk Information System, Before the Subcomm. on Oversight and Investigations of the H. Comm. on Science and Technology (Jun. 11, 2009)."

Figure 4: The current process.

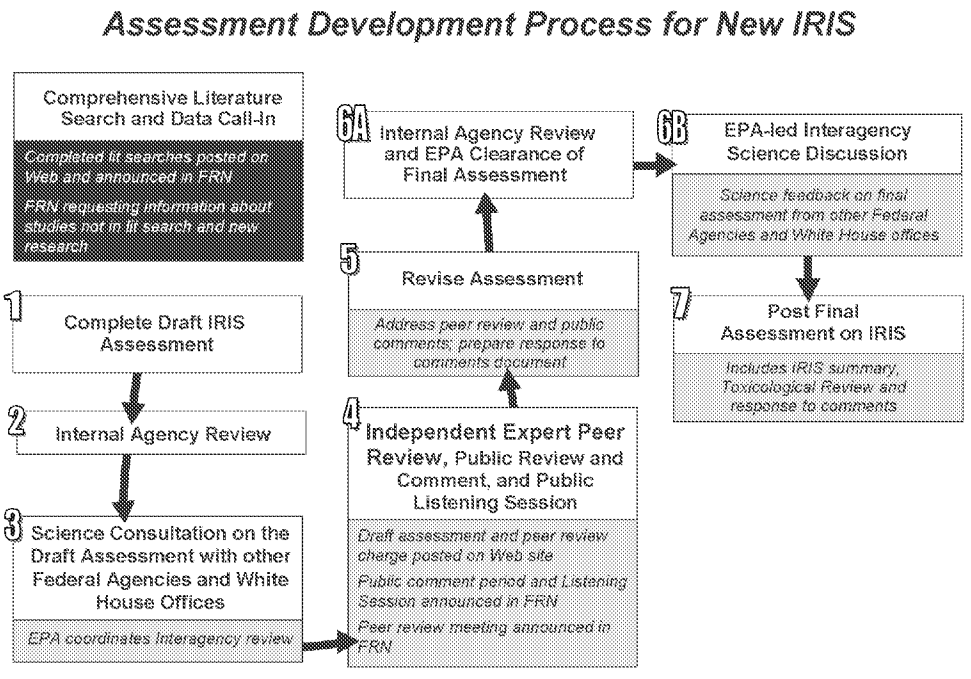

Figure 4: ENVIRONMENTAL PROTECTION AGENCY, NEW PROCESS FOR DEVELOPMENT OF INTEGRATED RISK INFORMATION SYSTEM (May 21, 2009), available at http://epa.gov/iris/process.htm.

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Improving the Process for Setting the IRIS Agenda

The principal purposes of the IRIS database are to identify hazards and help EPA and other agencies prioritize toxic substances that are of concern. The basic toxicology information contained in IRIS assessments along with other information collected by EPA, such as the Toxics Release Inventory, provide a basis for making decisions about chemical management. But the risk management process has its own set of procedural requirements for determining how best to protect the environment and public health from hazards related to toxic chemicals. These decisions are essentially separate from the risk assessment process, and need not be made during the IRIS process.

Given the gaping holes in the IRIS database, it is essential that EPA develop and pursue a well-considered process for completing the assessments necessary to complete IRIS profiles. That process ought to reflect communication and cooperation between IRIS staff and other EPA program officers, it ought to seek to balance of statutory needs and priorities of the program offices, and it ought to be transparent so that the public and various stakeholders will know what is under consideration. So far, however, EPA has focused on a few high-profile IRIS assessments, without offering up to the public any explanation for why these assessments have been chosen at the expense of others.

EPA program offices that regulate toxic substances rely heavily on IRIS assessments to help carry out their statutory responsibilities. The CAA's HAPs program regulates emissions of toxic substances.[12] Under the program, EPA establishes standards for sources of toxic air pollutants and then determines the residual risk associated with these substances once industry implements the regulations. EPA program staff makes residual risk determinations based on health hazard analyses, exposure data, and dose-response characterizations.[13]

The IRIS database should provide key information for those determinations, but it has critical data gaps. **Thirty-two of the 188 HAPs listed in the CAA have no IRIS assessment at all, and 77 pollutants are listed in IRIS but do not have inhalation risk information**. As a result, EPA cannot easily evaluate residual risk for 109 of 188 listed substances.

Similarly, EPA program staff's implementation of the SDWA relies on human health information for prioritizing substances to set primary drinking water standards. Their work is also dependent on public health information for health risk reduction and cost analysis in setting standards. Quantitative risk information is supposed to be included in IRIS, and, indeed, IRIS provides information on all but three substances currently regulated under the SDWA. In addition, 64 substances that have been nominated for regulatory consideration do not have IRIS assessessments. Included in the most recent Contaminant Candidate List are a range of pesticides and estrogen-like hormones for which there are no IRIS profiles.[14] These missing assessments, as with HAPs, hinder EPA's work in implementing the SDWA.

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IRIS is also critical in cleaning up Superfund sites. EPA guidance for using human health information in risk assessments for Superfund states that if an IRIS assessment is available, EPA need not seek out additional human health information.[15] **Unfortunately, IRIS assessments are not available for 87 of the 275 high-priority substances the Agency for Toxic Substances and Disease Registry (ATSDR) identified in 2007.** For these substances, EPA must look to other sources and make determinations about the quality of the information before a risk assessment can be completed. Risk assessments are used to determine whether cleanup action is warranted, to establish protective cleanup levels, and to estimate residual risk after cleanup.

The IRIS database should be a resource for other program offices. The IRIS staff should encourage open communication with other program offices to ensure that the IRIS database is most useful to the program offices. For example, the CAA Amendments of 1990 direct EPA to develop emissions standards for 188 specific HAPs, and then assess the "residual risk" posed by the pollutants after industry has instituted the pollution controls needed to meet the standards. The law provides only limited guidance to EPA on which assessments to undertake first. The Office of Air and Radiation should consult with IRIS staff to help develop such priorities.

EPA has generally provided lists of substances whose IRIS assessments had been completed in the previous year, new substances nominated for assessment in a specific year, and ongoing assessments that EPA expected to complete that year.[16] In 2009, EPA only provided information about substances for which literature searches had been completed.[17] EPA provides additional information about the progress of assessments through IRISTrack, but does not provide detailed information about how it has selected and prioritized assessments, nor does it explain its strategy or goals for working through the large number of assessments indicated by program offices.

The Obama administration has expressed a commitment to transparency through the Open Government Directive, which lays out several goals for improving transparency, including publishing information online, creating a culture of open government, and making legislative, budgetary and regulatory materials more accessible. EPA should explain its priorities for the IRIS program and account for data gaps on substances program offices need to carry out their missions. In effect, EPA is providing data without providing the underlying rationale for its decision-making, defeating the objective of the President's transparency initiative.

Recommendation

EPA should publish a clearly articulated IRIS agenda in the *Federal Register* each year. It should describe in its agenda how it plans to complete the large number of assessments needed to make the database current. When EPA develops this plan, it should give consideration, where possible, to conducting assessments of similar or related chemicals

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at the same time. The agency should divide the assessments into groups based on factors related to how complex they will be to complete and use those groupings to divide the workload more evenly. EPA should also explain how it will complete high-profile assessments without preventing the agency from completing all the other assessments.

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Removing the Barrier of Interagency Review

The interagency review process is a significant contributor to delay of IRIS assessments. From 2003 to 2007, the number of full-time staff devoted to IRIS rose from 10 to 35. In this period, the number of draft assessments set for interagency review rose from zero to 15, but the number of completed assessments was relatively stagnant – with five assessments completed in 2003 but just two in 2007.[18]

Not only does the interagency review process contribute greatly to gumming up the works of IRIS assessments, it also gives agencies that are themselves potentially regulated entities the opportunity to assert undue influence or delay assessments by years or even decades. The Department of Defense (DOD), for example, is the nation's biggest polluter, yet the interagency review process affords it a preferred seat at the table in establishing standards by which it will be regulated, something no corporate polluter could even hope to achieve.

Interagency review not only slows IRIS assessments, it also lets agencies that are potentially regulated push for favorable standards and cause delay.

In her 2009 reforms, Administrator Jackson chose to keep in place two opportunities for interagency review. The first is what is labeled "Step 3" in the new process: "Science consultation on the draft assessments with other Federal Agencies and White House Offices."[19] In a 2009 report, GAO noted that EPA's use of the phrase, "White House offices," is vague, and does not provide sufficient information about what White House offices are to be involved in this process. But based on the interagency review comments available for substances assessed under the new process, the White House Office of Management and Budget (OMB) seems to be the main driver, notwithstanding the fact that it only employs two professional scientists. The second opportunity for interagency review in Administrator Jackson's 2009 process is labeled, "Step 6B," "EPA-led Interagency Science Discussion." In brief, with this reform, Jackson asserted EPA control over the interagency review process, where previously OMB coordinated interagency review through OIRA.

The core problem with interagency review is that it provides agencies that may have conflicts of interest an opportunity to influence and delay risk assessments under the IRIS process. One example is the reassessment of trichloroethylene, long-term exposure to which has been linked to liver and kidney cancer and nerve damage. The substance is used as an industrial degreaser by many industries, as well as by the DOD, Department of Energy (DOE) and National Aeronautics and Space Administration (NASA). In 2004, EPA commissioned a joint study from the National Academy of Sciences (NAS) with DOD, DOE, and NASA on human health effects of trichloroethylene.[20] In response to the NAS report, NASA released a bulletin discussing the potential impact of regulatory actions related to trichloroethylene, including clean-up action.[21] NASA and other agencies were then given an opportunity to comment on the trichloroethylene draft assessment, a plain conflict of interest for the agencies, since the agencies themselves, and their contractors, are subject to the eventual regulation. Of course, public and private polluters are entitled to offer their views and provide information to regulators during the public comment period. The issue here is whether polluters should be given an up-front opportunity to comment on EPA scientists' findings about the hazards of the pollutants they discharge.

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As that example demonstrates, the interagency review process provides other federal agencies with a disruptive opportunity to inject policy considerations into the scientific assessments developed under IRIS. For example, this year, OMB submitted comments to the 2,3,7,8-tetrachlorodibenzo-p-dioxin (dioxin) reassessment expressing its disappointment that EPA did not calculate a "margin of exposure" in proposing a reference dose (RfD) for dioxin.[22] OMB argued: "Because the exposures of a proportion of the U.S. population would be above any RfD, it would have been useful for EPA to define the nature and magnitude of the risks at different levels of intake, the groups of the population most at risk, and the major sources of exposure for any at-risk groups." But decisions about whether and how to subdivide the exposed population for purposes of an IRIS assessment are science policy choices that do not belong in the IRIS process. These decisions should be made through the regulatory process, based on the strength of data and other factors without influence from potentially regulated parties, whose policy views are likely more informed by potential cleanup costs than by unbiased scientific considerations.

By retaining this interagency review process, EPA signaled that it continues to support the treatment of IRIS assessments as if they were themselves regulatory actions, rather than the scientific underpinnings for subsequent regulatory actions. For example, interagency review panels often call for additional explanation of factors related to regulatory action. In comments on the draft dioxin assessment, agencies asked for EPA to provide additional support for toxicity equivalent factors, which EPA explained were not used for the purposes of making IRIS assessments, but would be useful for future regulatory applications.[20] EPA leadership of the interagency science review process should have resulted in better balancing of EPA's interests with those of other federal agencies, but since the new IRIS process took effect, interagency comments have still resulted in delay, additional layers of analysis and calls for more and more science review.[23] The additional information supplied by federal agencies could be provided during a public comment period, so the delay created by interagency review does not justify the value of additional information shared by agencies.

A second problem with interagency review is that it provides additional avenues for industry interests to influence or delay the IRIS process. Industry interests commonly devote substantial resources to exploiting procedural opportunities to slow the process. And indeed, delay is at least a partial victory for industry, because assessments often provide significant basis for future regulations on toxic substances. As long as an industry can produce the appearance of a controversy around a substance, it can delay any regulatory action, and put off the day when it will have to conform to stricter regulation.

Industry tactics for delaying IRIS assessments are the product of years of experience fighting regulations. The guiding principle for delaying regulations and any government action that would protect people from hazards is to create a public perception of uncertainty in the link between chemical exposure and adverse effects. Industry has used this strategy for decades to delay regulations, win less stringent controls, and generate skepticism about

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science from the agencies, including EPA.[25] Although industry manufactures this sense of doubt in many ways, at the core, each tactic is related to the overarching strategy of delay.

Recent actions by the American Forest and Paper Association (AF&PA) and the Methanol Institute exemplify how industry can manipulate the interagency review process to sow doubt and promote regulatory delay. EPA posted its original IRIS profile for methanol in 1988. The agency updated the profile in 1993, however it still lacks the two most critical data points for a CAA HAP—an inhalation reference concentration and a cancer slope factor. In 2002, EPA began the process of developing these numbers, and by 2009 had come up with a draft of a new profile. At that point, AF&PA and the Methanol Institute instituted a coordinated attack on EPA's draft. AF&PA attacked the individual studies EPA used to support the new inhalation reference concentration and the new cancer slope factor.[26] The Methanol Institute took on the studies that EPA used to support the overall conclusion that methanol is likely to be a human carcinogen.[27] Those studies were conducted by the Ramazzini Institute, an Italian lab that specializes in long-term carcinogenesis studies that industry believes overestimate chemicals' carcinogenic potential. In its comments attacking the Ramazzini methanol studies, the Methanol Institute went so far as to demand an audit of the lab. Soon thereafter, the National Toxicology Program (NTP), an interagency program housed in the Department of Health and Human Services, made a visit to the Ramazzini labs and issued a report that was critical of the labs' pathology practices.[28] The report also suggested that EPA conduct additional review of the Ramazzini results used in various IRIS profiles. Immediately after receiving the report, EPA announced it would suspend its assessment of methanol and three other chemicals currently under review in the IRIS program.[29]

The agency could devote more resources to completing assessments if IRIS staff was not developing draft assessments to clear interagency hurdles.

The delay brought on by NTP's review of the Ramazzini labs may be evidence of a shrewd manipulation of the interagency review process by affected industry. At the very least, it will provide them with the opportunity to dump additional studies that they have funded into the docket. For instance, AF&PA hired a consulting company to conduct a review of EPA's draft IRIS assessment for methanol. The company, Exponent, has a long history of science for hire that stretches back to tobacco industry efforts to generate research to discredit the connection between smoking and cancer.[30] Since then, Exponent has been involved in a number of high-profile, industry-sponsored efforts to create a public perception that research linking products to hazards is controversial, including tests of laminated glass for Ford, which the company uses in litigation.[31] Such industry-sponsored studies are not subject to the guidelines set by the agencies and OMB for "quality, objectivity, utility, and integrity." Indeed, regulated industry has significant incentives to pay for studies that challenge agency results that recommend regulation. Such studies affect the IRIS process in two major ways – they slow it by requiring agencies to respond to petitions for correction of information, and they foster a perception of scientific disagreement. Industry interests have several opportunities to critique and discredit government science, but agencies are not provided with the same capacity to critique and re-analyze research presented from outside entities.

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Public access to federally funded research is much greater than privately funded research. Under the Data Access Act, federally funded research is subject to the Freedom of Information Act, giving private entities the opportunity to request underlying data and other information about federally funded studies. But privately funded studies are subject to no such disclosure requirements. As a result, industry-funded studies like the one conducted by Exponent for the AF&PA are effectively shielded from scrutiny by the media, the public, public interest organizations, and even the agencies themselves.

Without such checks on their work, there can be little assurance that industry-funded research meets the high standards of quality, objectivity, and independence required for use in the IRIS program. For instance, AF&PA also attached to its comments a study critical of EPA's assessment published in the journal *Regulatory Toxicology and Pathology*. The journal is sponsored by the industry-funded International Society of Regulatory Toxicology and Pharmacology, and has been criticized by a group of toxicologists for lacking transparency and editorial independence.[32]

One straightforward way to reduce the likelihood that bought-and-paid-for research finds its way into the IRIS process is to require a simple conflict disclosure, modeled after existing conflict disclosures adopted by scientific journals. Conflict disclosure would allow EPA, other agencies, and outside observers to quickly and easily consider potential conflicts of interest and account for any bias that might be built into industry-sponsored studies.[33] Apart from the problem of conflicts of interest, industry's ability to delay the regulatory process using research that is difficult to verify undermines EPA's ability to do its job in a timely manner.

In short, the interagency review process delays assessments without contributing to the IRIS process in a productive way. EPA expends resources in responding to interagency review comments and refining assessments multiple times before they are made available to a broader public for further comment. The agency could devote more resources to completing assessments if IRIS staff was not developing draft assessments to clear interagency hurdles—concerns that are often motivated by risk management concerns that are more appropriately raised during the development of actual regulations, rather than the development of a scientific assessment of possible harms. In addition, because EPA divides the review process into multiple steps, each of which requires EPA to wait and then re-evaluate its assessment, the agency sometimes is forced to respond to the same objections more than once.

Recommendations

The interagency review process should be eliminated and agencies should be given an opportunity to comment during a public comment period that is made equally available to all stakeholders. If significant science issues are raised in these public comments, EPA could then choose to initiate a more formal process for agencies to share information and resolve disputes.

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In addition, EPA should assert more authority to question or re-analyze industry-sponsored research or at least to be able to take conflicts of interest into account when considering weight-of-the-evidence determinations about toxic substances. A conflict disclosure requirement that provides information about identity of sponsors, what kind of support they provided, the role of the sponsor in the research process, and the sponsors' level of control over the study and data, would enable EPA to make such assessments.

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Limiting Redundant Review

In her 2009 memo announcing the new IRIS process, Administrator Jackson wrote that EPA would occasionally seek outside scientific review from the NAS and EPA's Science Advisory Board (SAB), but only in high-profile assessments of major importance.[34] Since then, however, EPA has chosen to focus the bulk of its IRIS energies on a handful of high-profile assessments, with the result that six assessments expected to be completed this year have been recommended for SAB review: dioxin, arsenic (inorganic), arsenic (non-cancer effects), trichloroethylene, polycyclic aromatic hydrocarbons, and methanol. Half of these assessments have already been reviewed by at least one outside panel of scientific experts: inorganic arsenic, dioxin and trichloroethylene have had SAB reviews previously. Inorganic arsenic was previously reviewed by the SAB from 2005-2006. Dioxin was previously reviewed by SAB in 1995 and by NAS in 2006. Trichloroethylene was previously reviewed by SAB in 2001 and by NAS in 2006. Often OMB encourages these science advisory board meetings during the interagency review process.[35]

To be sure, NAS and SAB review can add an additional layer of scientific expertise to the process. But it is a process that has already incorporated the expertise of EPA scientists, who are, among other things, assessing existing scientific literature based on expert research. In addition, the extra layer of review comes at the cost of greatly slowing down the process, sometimes by years. In the case of trichloroethylene, the two SAB reviews have taken nine years – the first SAB review was initiated in 2001, and the second SAB review has not yet been completed.

Between the outside peer review process, public comments and additional reviews of EPA's scientific judgment delay assessments by focusing on details that may not be relevant to the risk assessment task at hand, and contribute to cascading delays, making delay of assessments so lengthy that new research emerges in the interim, requiring EPA to start again from the beginning. All scientific questions can be studied virtually indefinitely. At some point, assessments must be entered into the IRIS database so that regulators can get to work protecting the public from harm. While it is important that IRIS assessments provide the best available scientific information, the science advisory process furthers the myth that IRIS assessments can be static answers about human health effects. EPA's decision to wait for unassailable answers undermines the goal of IRIS to be broadly informative. In addition, redundant layers of review can have a demoralizing effect on EPA staff that prompts them to rely only on the most deeply entrenched studies preventing them from incorporating new research.

EPA could easily incorporate more expert advice without halting the process to wait for additional SAB and NAS review, by inviting additional experts to comment on individual assessments as part of the public comment period. Instead of asking these experts to come to a consensus opinion, as NAS and the SAB do, EPA could simply solicit opinions and comments on any problems with EPA's draft. This would keep the assessment process

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moving forward and would prevent peer review from delaying the process. Including such comments in the public comment process would also promote transparency of the peer review process. Comments from outside experts would be published to a docket for the assessment and therefore could be reviewed by all interested parties.

Recommendations

EPA should attempt to limit SAB review to the greatest extent possible. There will be difficult and complicated assessments, where input from the SAB may add value, reduce conflicts and provide EPA staff with needed oversight and outside expertise. But EPA should strive to avoid multiple reviews by SAB and NAS. Further, EPA should make decisions about how and when it will consult outside scientific expertise, not OMB. One place where outside science review could add genuine value is when broader scientific questions are raised, such as the development of toxicity equivalence factors, which compare the relative toxicity of individual chemicals within a family of similar chemicals, or review of classes of chemicals. In these cases, the expert opinions and additional guidance to EPA provides clear added value, as such determinations are complex and may require additional scrutiny, particularly in cases where EPA is evaluating techniques or approaches it has not used previously.

If and when EPA program offices act on IRIS information and propose a regulatory action, specific procedures under the Administrative Procedure Act, executive orders governing review of regulatory actions, and statutory requirements under each specific statute should govern the promulgation of regulations. This process is well-developed and provides regulated industry and other stakeholders with ample opportunity to evaluate EPA's proposal and present information and perspectives to the process. EPA should forgo outside science review aimed at resolving questions that are related to potential regulatory actions or risk management decisions, rather than to the science underlying those decisions.

A nimbler IRIS process would also make it easier for EPA to revise assessments if new research becomes available. In fact, EPA staff undertook the task in 2003 of identifying assessments in the IRIS database that should be revised because of new research.[33] At its best, the IRIS database should be responsive to new information, and be flexible enough that that EPA can incorporate new information to existing assessments relatively quickly. Because other program offices rely so heavily on information in the IRIS database, EPA should err on the side of information and provide the greatest possible amount of information that is scientifically credible.

In short, expert peer review can be an important tool for supporting the findings of EPA, but the agency should strive to keep redundant reviews of IRIS assessments by outside science advisory boards to an absolute minimum.

While it is important that IRIS assessments provide the best available scientific information, the science advisory process furthers the myth that IRIS assessments can be static answers about human health effects.

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Putting EPA's Resources to the Greatest Effect

EPA's IRISTrack program paints a compelling portrait of just how much work remains before IRIS is truly current. A compilation of status reports on EPA's IRIS assessments currently in progress, IRISTrack shows that 67 IRIS assessments are currently in process, while 255 substances need assessments for EPA program offices to fulfill statutory mandates, and 169 substances currently listed in the database have been identified by EPA staff as being in need of updating to account for new information. EPA must complete a significantly greater number of assessments each year to quickly clear the backlog of assessments. If EPA were to complete these assessments in five years, it would have to complete approximately 84 assessments each year – nine times the number of assessments per year that it completed in the past year. Assessments cost money, and even if EPA streamlines its process along the lines recommended in this paper, the agency will require an increase in its IRIS budget from its current level of $14.5 million to approximately $100 million, with a commensurate increase in the number of full time staff to allow EPA to complete enough assessments for the database to stay current.

Although the IRIS program has received increases in funding and staff since 2000, it has not been able to complete enough assessments to meet the needs of EPA program officers and other users of the database. The low level of productivity of the IRIS program was the subject of House Science Committee hearings in 2009. The briefing memo for the hearing suggested that 20 assessments per year was the bare minimum level of productivity for the IRIS database to be relevant.[37] Even that is, in all likelihood, an understatement of what is needed. To complete the 478 assessments listed above at the rate of 20 per year would take 24 years. If the schedule includes the 77 HAPs listed but still missing inhalation values, it would take EPA 25 years to complete all the statutorily-indicated assessments, without taking on any new assessments. By contrast, at EPA's current pace of nine assessments per year, it will take 55 years for the IRIS program just to clear its backlog.

Simply dumping more money into the IRIS program will not fix the problem. EPA must make more effective use of its resources. In fiscal year 2010, the IRIS program received $5 million additional dollars and 10 additional staff to carry out its work.[38] In 2010, six assessments were referred for interagency review, eight are expected to complete the draft development phase, and EPA expects to complete nine assessments this year.[39]

The unfortunate reality is that EPA's new process for completing IRIS assessments has not addressed root causes of delay: the interagency review process, interference from regulated industry, excessive and redundant science review and inadequate strategic planning. Ideally, EPA would strive to reduce burdens on the assessment development process by focusing on a smaller number of key goals: reviewing toxicology information on toxic substances and providing an opportunity for peer review and public comment on the agency's assessment. Reducing these burdens would ensure that interested parties would have an opportunity to participate in the assessment development process and provide key oversight consistent with the requirements of the scientific community.

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Recommendations

EPA should pursue two principal budget objectives with respect to IRIS. First, it should devote a limited amount of resources to high-profile IRIS assessments. Doing so would ensure that these high-profile or complex assessments are completed, but that they do not interfere with EPA's completion of other, easier-to-assess substances. The fraction of IRIS program resources devoted to high-profile chemicals should have a firm cap, so as to put an end to the current dynamic, in which EPA works on just a handful of the most difficult-to-complete assessments.

Second, EPA should develop a budget request that relies on a determination of what would actually be required to complete a target number of assessments. It should then add funding for ongoing assessments of high-profile substances. Such an approach would ensure that EPA would continue to complete assessments at a pace to keep the database up to date without high-profile assessments cannibalizing resources.

Administrator Jackson has an important opportunity to back up her assertion that the IRIS program is a key part of her chemical management strategy. The program needs sufficient resources and support so that the database can support the work of other program offices at EPA. Streamlining and simplifying the IRIS process would allow EPA to devote more of the agency's resources to completing assessments rather than responding to interagency comments and submitting to outside science review. If the agency divided priorities between a few high-profile assessments and a larger number of assessments that could be completed more quickly, EPA could complete more assessments while still making progress on the small number of high-profile assessments.

Finally, Congress should provide the IRIS program with the resources necessary to make sure IRIS is able to meet the needs of the program offices, and to keep the database up to date.

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Conclusion

The reforms to the IRIS program implemented by EPA in May 2009 have not made the IRIS program productive enough to support EPA's statutory responsibilities with respect to IRIS, or to the regulatory programs that rely on it so that they can do the important work of protecting Americans from toxic substances. In particular, by prioritizing a small number of high-profile assessments, retaining interagency review, and overusing NAS and SAB review, EPA has fallen into the trap of continuing the appallingly low completion rate for IRIS assessments.

EPA has the authority to implement all of these changes recommended in this paper, with the exception of funding requests that will require appropriation by Congress. EPA's principles for chemical management state that "[c]lear, enforceable and practicable deadlines applicable to the Agency and industry should be set for completion of chemical reviews, in particular those that might impact sensitive sub-populations."[40] Under the EPA's current IRIS process, there is no way to set a clear or enforceable deadline for chemical review. If Administrator Jackson wants to achieve a better, more protective chemical management strategy, it is imperative that the IRIS program become nimbler and better able to fulfill the needs of other offices at EPA to carry out their statutory responsibilities.

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[30] Michaels, Doubt is Their Product, *supra* note 25.

[31] Jayne O'Donnell, *Critics question Exponent's laminated glass tests*, USA Today, May 20, 2010.

[32] Axelson O, et al., *Correspondence regarding publication ethics and Regulatory Toxicology and Pharmacology*, 9 Int J Occup Environ Health 386–89 (2003). Industry interests that fund the International Society of Regulatory Toxicology and Pharmacology include: American Chemistry Council, Bristol–Myers Squibb Company, Dow AgroSciences, Eastman Kodak, Gillette Company, Indspec Chemical Corporation, Merck and Co., Inc., Procter and Gamble, R.J. Reynolds Tobacco Company, The Sapphire Group, Inc., Schering– Plough Research Institute, and SmithKline Beecham Pharmaceuticals.

[33] *See, e.g.*, Wendy Wagner & David Michaels, *Equal Treatment for Regulatory Science: Extending the Controls Governing Quality of Public Research to Private Research*, 30 Am. J.L. & Med. 149 (2004).

[34] EPA, New Process for IRIS *supra* note 3.

[35] *See, e.g.*, OMB Comments on *Draft TCE Toxicological Review*, *supra* note 24.

[36] Environmental Protection Agency, Screening-Level Review of Toxicity Information Contained in the Integrated Risk Information System (IRIS) Database (2003) (on file with authors).

[37] *H. Comm. on Science and Technology, Fixing EPA's Broken IRIS*, *supra* note 9.

[38] Environmental Protection Agency, FY 2010 EPA Budget in Brief, 45 (2009), *available at* http://www.epa.gov/budget/2010/2010bib.pdf (accessed Oct. 4, 2010).

[39] Environmental Protection Agency, IRISTrack, *available at* http://cfpub.epa.gov/ncea/iristrac/index.cfm (accessed Oct. 4, 2010).

[40] Environmental Protection Agency, Essential Principles for Reform of Chemicals Management Legislation (Sept. 2009), *available at* http://www.epa.gov/opptintr/existingchemicals/pubs/principles.html (accessed Oct. 4, 2010).

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Setting Priorities for IRIS:

47 Chemicals that Should Move to the Head of the Risk-Assessment Line

by CPR Member Scholar Rena Steinzor and
CPR Policy Analysts Matthew Shudtz and Lena Pons

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Setting Priorities for IRIS: 47 Chemicals that Should Move to the Head of the Risk-Assessment Line

Executive Summary

EPA's Integrated Risk Information System (IRIS) is the starting point for new regulations under the Clean Air Act (CAA), Comprehensive Environmental Response, Compensation and Liability Act (CERCLA) and the Safe Drinking Water Act (SDWA). Scientists in the IRIS office produce risk assessments of individual chemicals, which regulatory staff then combine with exposure data and statute-based policy choices to write new emissions limits and cleanup standards. In previous reports, the Center for Progressive Reform (CPR) has described massive gaps in the IRIS database, including more than 250 chemicals for which EPA's air, drinking water, and Superfund offices need robust risk assessments.[1] In this white paper, we describe how EPA should prioritize the work it will take to close those data gaps. We have developed a list of 47 chemicals that IRIS staff should move to the top of its list of priorities, based on the air toxics, drinking water, and Superfund program offices' most pressing needs.

Toxicology is predicated on the axiom that the dose makes the poison. IRIS profiles provide EPA, state and local public health officials, and the public with information about the relevant doses for hundreds of toxic substances. We recommend EPA improve its priority-setting process for IRIS by taking a two-step approach to deciding which data gaps to fill first. As a first step, EPA must foster better cooperation and communication between IRIS staff and their colleagues in the air, drinking water and Superfund program offices, to ensure that the priorities of risk assessors in the IRIS office parallel the priorities of risk managers in the program offices. Second, EPA should take environmental justice into consideration and determine whether there are patterns of unknown chemicals being emitted in large quantities in disadvantaged communities.

[1] CENTER FOR PROGRESSIVE REFORM, *Corrective Lenses for IRIS: Additional Reforms to Improve EPA's Integrated Risk Information System* (Oct. 2010), *available at* http://www.progressivereform.org/articles/IRIS_1009.pdf [hereinafter CPR, *Corrective Lenses for IRIS*].

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Table 1: Priority Chemicals List				
Air toxins	*Superfund pollutants*	*Drinking water contaminants*	*Multi-media threats*	*Environmental justice concerns*
Cadmium compounds	Polycyclic aromatic hydrocarbons	1,2-Diphenyl-hydrazine	Acetamide[1,3]	1,1,2-Trichloro-ethane[1,2,4,5]
Carbonyl sulfide	Arochlor 1260	1,3-Dinitro-benzene	4-Amino-biphenyl[1,2]	1,2-Dichloro-ethane[1,2,3,4]
Formaldehyde	Arochlor 1242	Acetochlor ethanesulfonic acid	Arochlors[1,2]	Chlorobenzene[4,5]
Hydrogen fluoride	Arochlor 1221	Acetochlor oxanilic acid	Chromium[2,3]	Diaminotoluene[4]
Lead compounds	Cobalt	Alachlor ethanesulfonic acid	Cobalt[2,3]	Hexachloro-benzene[4,5]
Mercury compounds	DDT, O,P'	Alachlor oxanilic acid	Ethylene oxide[1,3]	Hexachloro-ethane[1,3,4,5]
Methanol	Nickel	Diazinon	2,3,7,8-Tetra-chlorodibenzo-p-dioxin[1,2]	Methyl iodide[5]
Methylene chloride	Endrin ketone	N-Nitroso-dimethylamine (NDMA)	Vanadium[2,3]	Phthalic anhydride[2,3]
Nickel compounds	Chromium(VI) oxide	N-Nitroso-diethylamine (NDEA)		Quinone[2]
Phenol	Methane	N-nitroso-di-n-propylamine (NDPA)		Urethane[3]
		Terbufos		
			[1]Air, [2]Superfund, [3]Drinking water	Chemicals above are released in the following ZIP codes: [1]70734, [2]70805,[3]71730, [4]77541, [5]77571

In CPR's last paper on IRIS's information gaps, we identified 253 unique substances that need new or updated IRIS assessments.[2] In this paper, we selected the 47 substances from that list that EPA should move to the front of the line. The IRIS program staff are currently working on new assessments for just 17 of these 47 substances,[3] underscoring our concern that statutory priorities are not sufficiently factored into the IRIS agenda. The 47 unique substances listed in

[2] CPR, *Corrective Lenses for IRIS, supra* note 1, *at* 2-3.
[3] ENVIRONMENTAL PROTECTION AGENCY, *Integrated Risk Information System (IRIS); Request for Chemical Substance Nominations for 2011 Program,* 75 Fed. Reg. 63,827 (Oct. 18, 2010).

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Table 1 include: ten hazardous air pollutants (HAPs) in the greatest number of upcoming air toxics standards; the ten highest-scoring Superfund priority substances; 11 substances listed on the drinking water Contaminant Candidate List; eight substances that appear on more than one list; and the ten highest-emitting HAPs in areas with environmental justice concerns.

Introduction

EPA's three key statutes for regulating toxic chemicals in commerce are the Clean Air Act (CAA), the Comprehensive Environmental Response, Compensation and Liability Act (CERCLA), and the Safe Drinking Water Act (SDWA). These statutes share two characteristics that make environmental regulation complex: they are media-specific, which balkanizes the regulatory landscape; and they require EPA to quantify the risks of individual chemicals before setting regulations.

At present, EPA takes nominations for new chemical risk assessments from Deputy Assistant Administrators, Deputy Regional Administrators, federal agencies that participate in reviews of draft IRIS assessments, and the public, then uses six criteria to select chemicals for IRIS assessments from among the nominations. But this process has not been sufficient to push the IRIS office to complete assessments in time for EPA program offices to regulate toxic substances.

The priority setting process functions like a black box: We know the criteria EPA applies and we know which IRIS profiles are completed, but we do not know how EPA applies these criteria to the un-assessed and under-assessed substances to set IRIS priorities. Based on the large number of chemicals identified by program offices that have not been assessed, we can infer that EPA's current process is not prioritizing assessments to meet the program offices' needs.

In this paper, we propose a two-step process for prioritizing new chemical reviews in the IRIS program: first, risk assessors from the IRIS office and risk managers from the regulatory offices need to work together to develop a complete list of chemicals in need of IRIS assessments; second, the chemicals should be prioritized in terms of the existing regulatory agenda and environmental justice concerns.

EPA program offices provide public information about chemicals considered for regulation, which we have parsed to develop a list of 253 substances that could be the starting point for discussions between IRIS risk assessors and regulatory risk managers. The CAA HAPs have been public since the Clean Air Act Amendments of 1990 were made law; the Agency for Toxic Substances and Disease Registry (ATSDR), a program under CERCLA, periodically publishes a list of priority chemicals; and, under the SDWA, the Office of Water must publish a Contaminant Candidate List (CCL) every five years. This information gives the IRIS staff guidance about chemicals of concern to EPA, but does not help them to prioritize their work.

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Since IRIS staff cannot tackle all 253 substances at once, a more robust effort at coordination is necessary, including regular meetings between the staff and managers of all offices to set short- and long-term priorities. Those priorities should be informed by environmental justice concerns. Specifically, EPA should prioritize the assessment of chemicals that lack IRIS profiles and are emitted in large quantities in communities with significant populations of poor and minority residents and in localities where a large number of un-assessed chemicals are emitted together. In this white paper, we profile five communities that bear the burden of numerous un-assessed HAPs and multiple Superfund sites.

Improving priority-setting policies will put the IRIS staff on the right path, but the database will remain outdated without reforms to the assessment process. Potentially regulated parties, particularly industry and other federal agencies like the Department of Defense and National Aeronautics and Space Administration, have isolated IRIS as a choke point for regulation. Their opposition has resulted in an IRIS program that can neither keep up with the demands that have already been made, nor incorporate information about new substances. IRIS staff must consider new ways to avoid the problem of "information capture," whereby potentially regulated parties dump so much new data on the agency – and do so with such frequency – that new assessments become mired in continuous controversy.

Setting Priorities, Step One: Improving Communication between Regulatory Office and IRIS Staff

EPA program offices have specific deadlines and plans to complete regulatory actions on toxic chemicals. The IRIS staff should be well-attuned to the deadlines and priorities of the program offices, and strive to provide program offices with the best available risk assessment information in a timely manner to support regulatory decisions. There should be regular communication and interaction between the program office staff and IRIS staff to facilitate priority-setting and ensure that priorities are consistent with the needs of the program offices.

The next three sections provide some additional details about the three programs and some thoughts on prioritizing chemicals that are important to each program.

Hazardous Air Pollutants

The CAA Amendments of 1990 specify 188 toxic air pollutants that EPA must regulate through a two-step process. First, EPA must issue "technology-based" standards for all major sources of HAPs. At this stage, EPA staff simply determine emissions limitations based on the average emission limitation of the best performing 12 percent of existing sources. EPA has issued 96

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technology standards covering 174 "major" and "area" sources.[4] In the second step of the HAPs regulations, EPA must evaluate "residual risks" associated with air pollutants eight years after the technology-based standards are promulgated, in an effort to determine whether the technology-based standards protect public health with "an ample margin of safety."[5]

IRIS profiles are integral to the residual risk determinations. EPA considers an ample margin of safety to be exposures below the reference concentration (RfC or inhalation value) listed in IRIS for non-carcinogens, and the level at which added cancer risk does not exceed one in one million.[6] But the IRIS database is missing assessments or inhalation values for 107 of 188 HAPs, slowing progress toward completion of residual risk standards. In fact, EPA's Science Advisory Board (SAB) reviewed the Office of Air and Radiation's (OAR) methodology for completing two residual risk evaluations and implored EPA to complete IRIS profiles for all HAPs in a timelier manner.[7] They said that EPA's alternate method of determining risk was too simplistic, and recommended that EPA elaborate on the proposed method. But they stressed that the best course of action was to complete IRIS profiles for all the HAPs.

> Data gaps in IRIS's HAPs coverage stymie public health efforts led by state and local agencies, too. In 2005, the Mayor of Houston, Bill White, ordered a task force on air pollution in the area. Houston's Ship Channel is home to large number of petrochemical refineries and other chemical plants, and has high concentrations of a broad range of HAPs. The Task Force focused on 176 HAPs listed in EPA's 1999 National Air Toxics Assessment that were present in the 10 counties that comprise the greater Houston area. The researchers expressed difficulty in developing risk characterizations for Houston-area HAPs: "The intrinsic challenges of comparing HAPs-related health risks are illustrated by the fact that 118 (67%) of the 176 HAPs examined by the Task Force were assigned to the uncertain risk category. This decision was based on their collective judgment that there is insufficient evidence on hand to ascertain whether these substances currently pose a significant threat to the health and well being of Houston residents." Of the 118 HAPs placed in the uncertain risk category, 63 are missing IRIS profiles or lack inhalation values.

EPA completed the last of the technology-based standards in 2006, so it must issue all residual risk standards by 2014. With that deadline in mind, and with input from OAR, IRIS staff should set an agenda for completing risk assessments on all HAPs in an order that will pave the way for

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[4] ENVIRONMENTAL PROTECTION AGENCY, OFFICE OF INSPECTOR GENERAL, EVALUATION REPORT: KEY ACTIVITIES IN EPA'S INTEGRATED URBAN AIR TOXICS STRATEGY REMAIN UNIMPLEMENTED, Report No. 10-P-0154, (2010).
[5] 42 U.S.C. § 7412(f).
[6] *See, e.g.,* ENVIRONMENTAL PROTECTION AGENCY, *National Emission Standards for Coke Oven Batteries,* 70 Fed. Reg. 19,993 (Apr. 15, 2005).
[7] ENVIRONMENTAL PROTECTION AGENCY, SCIENCE ADVISORY BOARD. *Review of EPA's draft entitled, "Risk and Technology Review (RTR) Risk Assessment Methodologies: For Review by the EPA's Science Advisory Board with Case Studies – MACT I Petroleum Refining Sources and Portland Cement Manufacturing,"* SAB-10-007, *at* 5 (May 7, 2010) [hereinafter EPA, *RTR Methodology*].

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OAR's regulatory agenda. EPA has already finalized 16 residual risk standards and proposed or requested comment on 17 others. IRIS and OAR staff should work together to determine how the 13 HAPs covered by proposed standards but lacking key IRIS data could be assessed in time to meet OAR's regulatory timeline. A recent consent decree prompted by a Sierra Club lawsuit sets deadlines for 16 more residual risk standards that cover 114 HAPs—43 of which lack inhalation values in the IRIS database and should also be prioritized for review by IRIS staff.

CPR reviewed EPA's proposed rules and the 16 other standards which EPA must propose under the consent decree, and identified 123 HAPs in these upcoming standards.[8] Table 2 highlights the top 10 of those 123 HAPs, based on the number of upcoming rules in which they appear. The Appendix (Table A2) provides a longer list—all 46 HAPs that appear in upcoming standards but lack inhalation values or do not have IRIS values. Input from OAR would be valuable in improving the usefulness of this priority list. OAR needs IRIS profiles for HAPs to complete the residual risk standards, and OAR should share its needs with ORD, so IRIS profiles can be completed in a timely manner.

Table 2: Hazardous Air Pollutants with Insufficient IRIS Information in Upcoming Residual Risk Rules
Chemical
Cadmium compounds*
Carbonyl sulfide
Formaldehyde
Hydrogen fluoride*
Lead compounds
Mercury compounds
Methanol
Methylene chloride
Nickel compounds
Phenol
* *No IRIS profile information.*

Human Health Effects: Cadmium compounds

Cadmium compounds have been linked to kidney disease, lung damage, cancer, and fragile bones.

AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY, TOXFAQ FOR CADMIUM, (Sept. 2008), *available at* http://www.atsdr.cdc.gov/tfacts5.pdf (accessed Oct. 21, 2010).

[8] ENVIRONMENTAL PROTECTION AGENCY, *Risk and Technology Review, Phase II, Group 2,* 72 Fed. Reg. 14,741-14,744 (Mar. 29, 2007); ENVIRONMENTAL PROTECTION AGENCY, *National Emission Standards for Hazardous Air Pollutant Emissions: Group I Polymers and Resins,* 73 Fed. Reg. 60,437-60,440 (Oct. 8, 2008).

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Superfund Pollutants

Superfund is a critical part of EPA's overall mission. The Superfund program has a budget of $1.3 billion; it makes up 12 percent of EPA's total budget.[9] Cleanup standards for Superfund inform other waste management programs, including the Resource Conservation and Recovery Act and private-sector cleanup efforts. IRIS profiles are the first step in setting Superfund standards and initiating work that radiates beyond Superfund.

Superfund sites are places of significant soil and groundwater pollution, often by multiple contaminants. EPA prioritizes cleanup efforts based on whether contaminants pose an immediate hazard or a longer-term cleanup effort. Sites that are not marked for emergency response are added to the National Priorities List (NPL). After a site has been added to the NPL, it undergoes a seven-step process through which EPA oversees the remediation of a site, a process that begins with risk assessment.

The CERCLA requires ATSDR to periodically compile a list of "high priority" substances.[10] ATSDR generates this list from substances that are found in sites on the NPL. The list is placed in a weighted priority order that takes into account the frequency with which substances are found at sites on the NPL, the toxicity of the substance, and the likelihood of human exposure to the substance at a site. ATSDR provides the IRIS staff with quite a bit of useful information to make determinations about how to prioritize substances for IRIS assessment. ATSDR updates the list periodically, with new substances being added and others removed as the sites on the NPL change.[11] Nonetheless, many substances remain on the list for years, because they are common industrial chemicals, or are persistent environmental toxics. Even the longstanding high priority chemicals lack sufficient coverage in IRIS – 17 substances that have been on ATSDR's list since 1997 do not have IRIS profiles (*See* Appendix, Table A4).

> *Why ATSDR?*
>
> Dividing responsibilities across multiple agencies is one strategy to avoid agency capture. Congress created the ATSDR in 1986, after the integrity of EPA's Superfund program had been called into question by the actions of Reagan administration officials in charge of the program.

ATSDR's list, like the CAA's list of HAPs, provides an obvious indication of an EPA regulatory office's needs. But similar to its treatment of HAPs data gaps, EPA's IRIS agenda does not explain how it will address data gaps for substances on the ATSDR high priority list. There is no formal relationship between the ATSDR list and the IRIS agenda process. Research conducted

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[9] ENVIRONMENTAL PROTECTION AGENCY, FY 2010 EPA BUDGET IN BRIEF, 2, 6 (Apr. 2009) *available at* http://www.epa.gov/budget/2010/2010bib.pdf (accessed Dec. 15, 2010).

[10] 42 U.S.C. § 9604(i).

[11] AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY, CERCLA PRIORITY LIST OF HAZARDOUS SUBSTANCES, lists are available for 1997, 1999, 2001, 2003, 2005 and 2007, *available at* http://www.atsdr.cdc.gov/cercla/07list.html (accessed Sept. 16, 2010) [hereinafter ATSDR, CERCLA PRIORITY LIST].

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by ATSDR should flow freely between ATSDR and the IRIS program – indeed IRIS was created when EPA combined several disparate databases of human health information maintained by various program offices at EPA. The Superfund program should support IRIS to the extent that ATSDR is able to assist the IRIS program in completing assessments, identifying key studies, and making judgments about weight-of-the-evidence evaluations of toxic chemicals.

Table 3: Top Ten ATSDR Priority Chemicals not Listed in IRIS[12]

Chemical	*ATSDR points*[13]
Polycyclic aromatic hydrocarbons	1316.98
Aroclor 1260	1177.77
Aroclor 1242	1093.14
Aroclor 1221	1018.41
Cobalt	1015.57
DDT, O,P'	1014.71
Nickel	1005.4
Endrin ketone	978.99
Chromium(VI)oxide	969.58
Methane	959.78

Human Health Effects: Nickel

Exposure to nickel dust has been linked to respiratory problems including bronchitis and reduced lung function. Occupational exposures have been linked to lung and nasal cancer.

AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY, TOXFAQ FOR NICKEL, (Aug. 2005), *available at* http://www.atsdr.cdc.gov/tfacts15.pdf (accessed Oct. 21, 2010).

Drinking Water Contaminants

The Safe Drinking Water Act (SDWA) requires EPA to set standards for limits on drinking water contaminants. Unlike HAPs, which were specified by Congress, EPA is responsible for identifying water contaminants. EPA identifies additional water contaminants that might be candidates for regulation every five years by generating a new Contaminant Candidate List (CCL).[14] The lists contain recommendations both for chemicals and microbiological contaminants. Since 1996, EPA has published three CCLs that contain 156 distinct chemical substances.[15] IRIS profiles are missing for 64 (41 percent) of these substances. Absence of an IRIS profile hinders regulation of drinking water contaminants because the Water Office uses health risk information to prioritize unregulated substances to monitor, as well as determine what order to regulate water contaminants.

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[12] ATSDR, CERCLA PRIORITY LIST, *supra* note 11.

[13] Points are assigned by ATSDR is based on an algorithm that utilizes the following three components: frequency of occurrence at NPL sites, toxicity, and potential for human exposure to the substances found at NPL sites. *See* AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY, CERCLA PRIORITY LIST OF HAZARDOUS SUBSTANCES, WHAT IS THE CERCLA LIST, *available at* http://www.atsdr.cdc.gov/cercla/index.asp (accessed Sept. 19, 2010) [hereinafter ATSDR, WHAT IS THE CERCLA LIST].

[14] 42 U.S.C. § 300g-1(b)(1)(B)(i).

[15] ENVIRONMENTAL PROTECTION AGENCY, *Announcement of the Drinking Water Contaminant Candidate List; Notice,* 63 Fed. Reg. 10,273 (Mar. 2, 1998); ENVIRONMENTAL PROTECTION AGENCY, *Drinking Water Contaminant Candidate List 2; Final Notice,* 70 Fed. Reg. 9,071 (Feb. 24, 2005); ENVIRONMENTAL PROTECTION AGENCY, *Drinking Water Contaminant Candidate List 3 – Final,* 74 Fed. Reg. 51,850 (Oct. 8, 2009).

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The SDWA requires the EPA Administrator to make a public health finding about a contaminant before EPA moves to regulate the substance. The public health finding requires three determinations: first, EPA must establish that the contaminant may have an adverse effect on human health; second, the agency must determine that the contaminant is known or likely to occur in public water systems; and third, EPA must determine that regulation through SDWA presents a meaningful opportunity for reducing public health risks.[16] Reference doses contained in IRIS profiles are exactly relevant to the first determination. The IRIS program has not kept up with demand to provide information about CCL substances, which makes it more difficult for EPA to make the health risk related determinations required under SDWA.

Table 4 lists 11 of the 64 substances that appear in the CCLs that do not have IRIS profiles, culled from the larger list because they are also tracked under the Unregulated Contaminant Monitoring program. In the Appendix (Table A5), we identify nine additional substances EPA tracks under the Unregulated Contaminant Monitoring program that do not appear on the Contaminant Candidate Lists, but are missing IRIS profiles.

Table 4: UCMR Listed Substances also on CCL without IRIS profiles
Chemical
1,2-diphenylhydrazine
1,3-Dinitrobenzene
Acetochlor ethanesulfonic acid
Acetochlor oxanilic acid
Alachlor ethanesulfonic acid
Alachlor oxanilic acid
Diazinon
N-nitrosodiethylamine (NDEA)
N-nitrosodimethylamine (NDMA)
N-nitroso-di-n-propylamine (NDPA)
Terbufos

Human Health Effects: Ethylene Oxide

Ethylene oxide has been linked to miscarriage, respiratory and nervous system effects. Ethylene oxide is listed of programmatic importance both for safe drinking water and as a HAP.

AGENCY FOR TOXIC SUBSTANCES AND DISEASE REGISTRY, TOXFAQ FOR ETHYLENE OXIDE, (Jul. 1999), *available at* http://www.atsdr.cdc.gov/tfacts137.pdf (accessed Oct. 21, 2010).

[16] 42 U.S.C. §300g-1(b)(1)(A).

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Setting Priorities, Step Two: Considering Environmental Justice

IRIS staff can use the regulatory offices' legal obligations and administrative priorities to start the process of choosing which chemicals need new or updated assessments, but those two factors will still leave them with a substantial list. IRIS staff should further prioritize new assessments by taking into consideration environmental justice concerns.

Environmental justice, as defined by EPA, means "fair treatment and meaningful involvement of all people regardless of race, color, national origin, or income with respect to the development, implementation, and enforcement of environmental laws, regulations, and policies."[17] In practice, EPA's policy for ensuring environmental justice places an obligation on EPA staff to consider first, whether their actions disproportionately impact any group(s) of people, and second, whether all affected groups have a meaningful opportunity for involvement in the regulatory process.

In the IRIS assessment priority-setting context, IRIS staff could take into account the potential for disproportionate impacts by analyzing emissions and exposure data for the unassessed HAPs, CERCLA priority chemicals, and drinking water contaminants to determine where clusters of those unassessed chemicals can be found. Over the next few pages, we profile five communities where HAPs that have insufficient profiles are released in significant quantities. These five communities were chosen because they are sites with a large diversity of toxic air pollutants and have the largest number of HAPs without IRIS profiles. In addition to considering HAPs, we also looked at the presence of Superfund sites, and toxic chemical releases listed in EPA's Toxic Release Inventory (TRI). After we selected the communities, we probed basic demographic information from the 2000 Census, which is listed in the community profiles.

Our methodology is but one way that IRIS staff might take environmental justice into account when prioritizing new assessments. These communities are subject to diverse exposure to toxic chemicals through multiple pathways. We selected them based on the presence of the largest number of exposures to substances that are missing IRIS profiles, but these communities are also exposed to an even larger diversity of toxins.

One of EPA's long-term goals is to better understand the cumulative impacts of multiple toxins.[18] Chemical-by-chemical information contained in IRIS – oral exposure limits, inhalation values – is exactly the kind of toxicology information needed to complete cumulative risk

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[17] ENVIRONMENTAL PROTECTION AGENCY, OFFICE OF POLICY, ECONOMICS AND INNOVATION, EPA'S ACTION DEVELOPMENT PROCESS: INTERIM GUIDANCE ON CONSIDERING ENVIRONMENTAL JUSTICE DURING THE DEVELOPMENT OF AN ACTION (2010) *available at* http://epa.gov/compliance/ej/resources/policy/considering-ej-in-rulemaking-guide-07-2010.pdf (accessed Nov. 2, 2010).

[18] *See, e.g.*, Thomas Burke, *Overview of Cumulative Risk, presentation before Environmental Protection Agency, Mid-Atlantic Cumulative Risk Workshop* (2003), *available at* http://www.epa.gov/region3/environmental_justice/cumriskwkshop.htm (accessed Dec. 1, 2010).

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analysis. Cumulative risk assessments are highly dependent on toxicology information about each of the various toxic substances and exposure pathways. If toxicology information is not present, then the evaluation cannot be credibly completed. Cumulative risk assessments become less credible as the number of data gaps increase. EPA must identify both where there is a large diversity of exposure to toxic substances, and which toxic substances that appear in these areas are missing critical toxicology information. The IRIS office should then strive to prioritize substances that hinder cumulative risk assessment.

EPA's environmental justice policies also require that staff consider whether all affected groups are able to meaningfully participate in program decisions. IRIS staff can help more groups participate more meaningfully in the regulatory process by finalizing new chemical profiles for toxins that appear in communities like those profiled below. These communities often have limited resources to devote to participation in the highly technical standard-setting and permitting decisions that affect the quality of their air, water, and soil. The existence of IRIS profiles for all relevant chemicals helps these communities advocate for themselves. The IRIS office should strive to support environmental justice by identifying unassessed chemicals from our list that appear in communities that are not adequately included in the decision making process.

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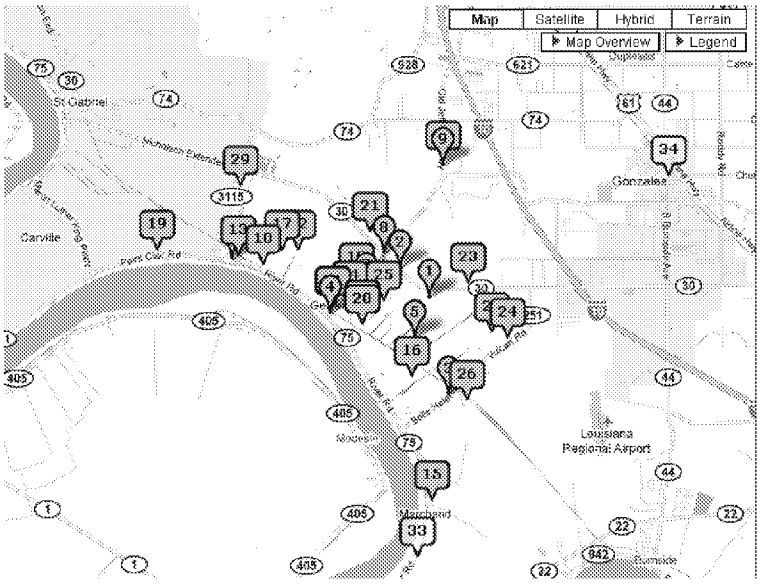
Geismer, LA 70734
Ascension Parish



Geismer, Louisiana is located about 30 miles south of Baton Rouge. It is home to a large number of petrochemical facilities, including the largest manufacturing facility for the chemical company BASF. According to EPA's Toxic Release Inventory, residents of Geismer are exposed to 94 toxic chemicals.

Blue markers represent sources of air pollution. Yellow markers are Superfund sites.

Toxics Release Inventory Information for 70734				
Total Releases (lbs)	*Air Releases (lbs)*	*Water Releases (lbs)*	*Land Releases (lbs)*	*Transfers to Off-Site Treatment Works (lbs)*
9,522,750	2,530,641	6,738,084	27,569	226,457

Sources of Toxic Substance Exposures for 70734 and Ascension Parish		
Air toxics not in IRIS	*Superfund sites (70734)*	*Superfund sites (Ascension, LA)*
14	2	5

Demographics Information for Geismer and Ascension Parish		
	70734	*Ascension Parish*
Race		
White	58.7%	77.6%
Black	36.9%	19.8%
Native American	0.0%	0.4%
Asian	1.6%	0.4%
Pacific Islander	0.0%	0.0%
Hispanic/Other	0.4%	0.9%
Median household income	$39,336	$44,288
% below poverty line	12.9%	12.8%

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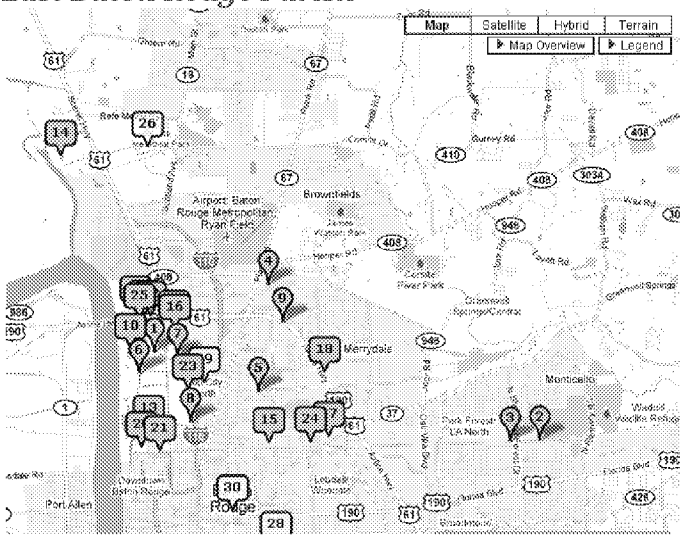
Baton Rouge, LA 70734
East Baton Rouge Parish



Baton Rouge is the capital of Louisiana. It lies on the Mississippi River, about eighty miles west of New Orleans. Baton Rouge is home to a deepwater port connecting the Mississippi River to the Gulf of Mexico. Major industries in Baton Rouge include petrochemical production, plastic, rubber, and timber and paper products, which contribute to air and water pollution in the area. According to EPA's Toxics Release Inventory, residents of Baton Rouge are exposed to 116 different toxic chemicals.

Blue markers represent sources of air pollution. Yellow markers are Superfund sites.

Toxics Release Inventory Information for 70805				
Total Releases (lbs)	*Air Releases (lbs)*	*Water Releases (lbs)*	*Land Releases (lbs)*	*Transfers to Off-Site Treatment Works (lbs)*
9,961,982	4,725,250	5,089,631	250	146,851

Sources of Toxic Substance Exposures for 70805 and East Baton Rouge Parish		
Air toxics not in IRIS	*Superfund sites (70805)*	*Superfund sites (East Baton Rouge Parish)*
12	1	18

Demographics Information for Baton Rouge and East Baton Rouge Parish		
	70805	*East Baton Rouge Parish*
Race		
White	10.7%	51.8%
Black	86.8%	44.5%
Native American	0.2%	0.3%
Asian	0.8%	2.5%
Pacific Islander	0.0%	0.0%
Hispanic/Other	0.5%	2.8%
Median household income	$21,203	$42,173
% below poverty line	34.2%	17.6%

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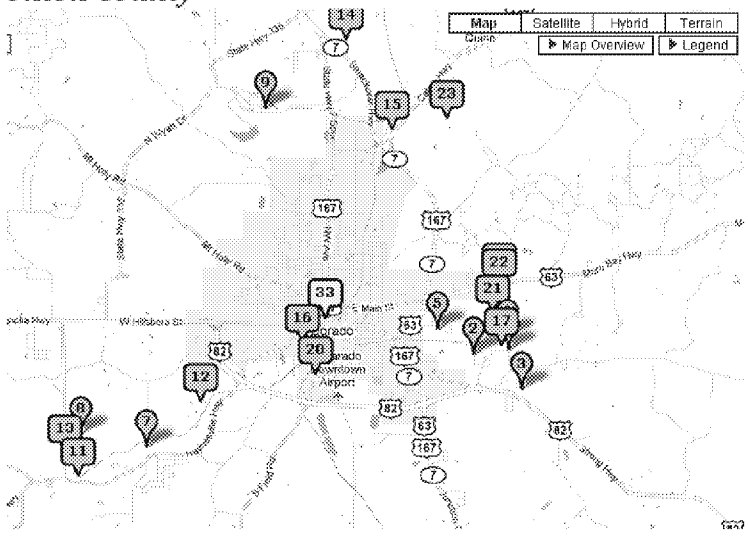
El Dorado, AR 71730
Union County



El Dorado, Arkansas is located in the southern part of the state, near the Louisiana border. It was once a site for oil extraction. More recently it is the home to a diversity of chemicals manufacturing, including agricultural chemicals, automotive chemicals, pesticides, bleaching agents and synthetic dyes. The town of El Dorado contains six Superfund sites. EPA estimates residents of El Dorado are exposed to 177 toxic chemicals.

Blue markers represent sources of air pollution. Yellow markers are Superfund sites.

Toxics Release Inventory Information for 71730				
Total Releases (lbs)	*Air Releases (lbs)*	*Water Releases (lbs)*	*Land Releases (lbs)*	*Transfers to Off-Site Treatment Works (lbs)*
7,749,243	1,209,550	4,369,657	1,464,241	705,794

Sources of Toxic Substance Exposures for 71730 and Union County		
Air toxics not in IRIS	*Superfund sites (71730)*	*Superfund sites (Union County)*
14	6	7

Demographics Information for El Dorado, AR and Union County		
	71730	*Union County*
Race		
White	66.2%	64.8%
Black	31.6%	33.1%
Native American	0.3%	0.3%
Asian	0.4%	2.5%
Pacific Islander	0.0%	0.0%
Hispanic/Other	0.5%	2.8%
Median household income	$30,565	$37,120
% below poverty line	18.8%	18.6%

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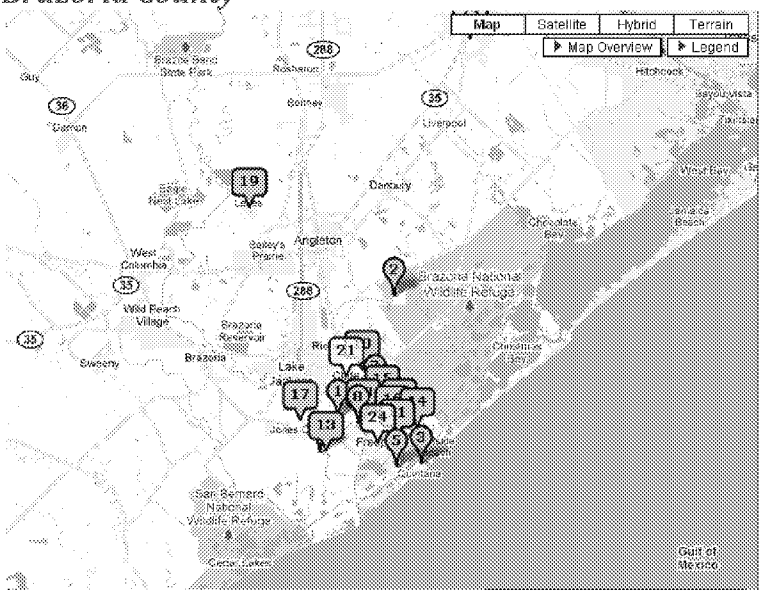
Freeport, TX 77541
Brazoria County



Freeport, Texas is located on the Gulf of Mexico coast south of Houston. It is home to a deepwater port and large-scale petrochemical manufacturing. Freeport also maintains a liquefied natural gas terminal. These sites are major sources of air pollution in Freeport. EPA reports that residents of Freeport are exposed to 136 toxic chemicals.

Blue markers represent sources of air pollution. Yellow markers are Superfund sites.

Toxics Release Inventory Information for 77541				
Total Releases (lbs)	*Air Releases (lbs)*	*Water Releases (lbs)*	*Land Releases (lbs)*	*Transfers to Off-Site Treatment Works (lbs)*
5,377,060	2,452,712	2,535,381	69,489	319,470

Sources of Toxic Substance Exposures for 77541 and Brazoria County		
Air toxics not in IRIS	*Superfund sites (77541)*	*Superfund sites (Brazoria County)*
9	2	10

Demographics Information for Freeport, TX and Brazoria County		
	77541	*Brazoria County*
Race		
White	83.5%	82.2%
Black	12.1%	11.2%
Native American	0.6%	0.6%
Asian	0.4%	4.6%
Pacific Islander	0.0%	0.0%
Hispanic/Other	19.8%	2.1%
Median household income	$33,933	$60,784
% below poverty line	23.5%	9.2%

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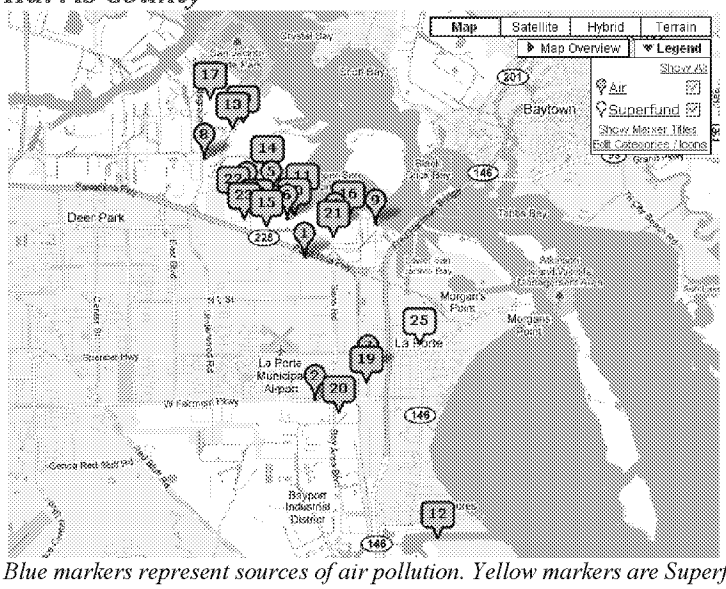
La Porte, TX 77571
Harris County



Blue markers represent sources of air pollution. Yellow markers are Superfund sites.

LaPorte, Texas is on Galveston Bay and is located in Houston's Ship Channel, which is home to a large number of petrochemical facilities. In 2005, the Mayor of Houston ordered a task force to investigate the effects of air pollution in the Houston area, including Harris County. Data gaps in IRIS hindered the task force's ability to assess health effects. In addition to air pollution, Harris County also contains 81 Superfund sites. According to EPA, residents of LaPorte are exposed to 279 toxic chemicals.

Toxics Release Inventory Information for 77571				
Total Releases (lbs)	*Air Releases (lbs)*	*Water Releases (lbs)*	*Land Releases (lbs)*	*Transfers to Off-Site Treatment Works (lbs)*
4,379,416	2,195,039	1,680,546	169,558	334,272

Sources of Toxic Substance Exposures for 77571 and Harris County		
Air toxics not in IRIS	*Superfund sites (77571)*	*Superfund sites (Harris County)*
16	1	81

Demographics Information for LaPorte, TX and Harris County		
	77571	*Harris County*
Race		
White	81.5%	73.5%
Black	6.7%	18.7%
Native American	0.6%	0.7%
Asian	0.7%	5.1%
Pacific Islander	0.0%	0.2%
Hispanic/Other	7.9%	1.3%
Median household income	$56,552	$42,598
% below poverty line	7.2%	15.9%

Streamlining the Process

Improving the priority-setting process for completing IRIS assessments is key to bringing the IRIS database up to date. But considering that EPA has such a large number of assessments to complete, it must also address how it manages its workload, and devise a process that allows the IRIS program to complete more assessments each year. EPA should streamline the process by setting goals for how many assessments to complete each year, drawing from substances of programmatic importance; eliminating the interagency review process; relying on outside science review only in the most complex cases; and preventing a few high-profile assessments from impeding progress on others by completing those assessments on a separate track with a separate budget.

In addition to structural problems with the IRIS process, regulatory agencies including EPA are plagued by information overload.[19] The regulatory process does not discourage—and actually encourages—interested parties to submit large volumes of unfiltered information to agencies. As a result, attention, not information, is in short supply in making regulatory decisions. The consequences of this overload of information include an increased cost of participation in the regulatory process – both to produce competing analyses and information and to review and understand information submitted by other interests. Industry interests, having more resources to participate in this process, dominate the process in terms of the amount of information submitted to agencies and critical evaluation of information submitted by other interests. This creates an echo chamber effect where agencies hear one perspective—industry's—much more often than others, creating a perception that the dominant perspective is the correct one.

This drop-off in pluralistic participation is described as "information capture."[20] By volume and frequency of participation, better-funded industry interests influence agencies in favor of the industry position. The IRIS program is subject to substantial information capture due to the complexity of the assessment process and the highly technical nature of its work. The IRIS office faces a prodigious backlog of assessments, and a stream of critique of its work. Industry has a strong incentive to flood the agency with more information than it can effectively process. Since there are no mechanisms in the regulatory process to limit interested parties from dumping raw data into the record, there is too much information for agency staff to read through. The agencies, battered by searching judicial review of their prior decisions, take it upon themselves to respond to the content of all the submissions made to the agency in the course of the regulatory process, in an attempt to insulate themselves against future litigation.

Although the IRIS process is not a regulatory process, it is subject to many of the same challenges in terms of information overload. ORD staff is inundated from the start with

[19] Wendy Wagner, *Administrative Law, Filter Failure, and Information Capture,* DUKE L. J. Vol. 59, (2010) [hereinafter Wagner, *Filter Failure*].
[20] *Id.*

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information. Before a draft assessment is published, ORD staff comb through the literature and produce a "screening-level literature review," which is then published in the *Federal Register* and opened for public comment. Industry and other interests, including other federal agencies, then submit additional studies and data that ORD staff must read and synthesize. Part of this process is motivated by industry's efforts to generate the appearance of controversy, a deregulatory tactic that dates from the tobacco industry's 1960s efforts to suppress and obfuscate the relationship between smoking and cancer.[21]

Information capture is not unique to the IRIS process. But with such a large backlog of assessments to complete, the IRIS process could be a good test case for strategies to reduce the influence of excessive information. Placing some manner of filtering requirement on interest groups, akin to limits placed by appellate courts on litigants, could provide some relief to agencies in addressing information overload.[22] Limits would encourage interested parties to point to specific studies or findings relevant to issues with IRIS assessments. EPA staff could then focus on a few problems and more quickly finish the weight-of-the-evidence determinations required for IRIS.

Conclusion

CPR's research has identified 253 substances awaiting IRIS assessments, an unacceptably high number. EPA's program offices need IRIS information to complete statutorily mandated tasks. EPA should set a goal for working through these assessments, and then submit a budget proposal that reflects the resources it would take to finish the work in that amount of time. Congress should then provide the IRIS program with adequate funding to complete the work. Although the current budget situation is such that many programs are being cut, our own back-of-the-envelope calculations estimate that the IRIS backlog could be cleared in five years for approximately $100 million. In the context of the federal budget, this is not an unbearable request. Indeed, it would amount to 0.003 *percent* of the $3.5 trillion in federal outlays from FY2009. The IRIS process should be reformed to remove roadblocks and reduce the amount of time it takes to complete assessments.

Moving forward, EPA should set priorities based on program office need, taking into consideration environmental justice factors. Some mechanism for setting the IRIS agenda based on expected needs of the program offices should be developed. The IRIS staff should determine how many assessments must be completed based on the need from the program offices, not based on the available budget. To the greatest extent feasible, program offices should give ORD advance notice of chemicals of interest, so the IRIS staff can integrate these substances into the

[21] DAVID MICHAELS, DOUBT IS THEIR PRODUCT: HOW INDUSTRY'S ASSAULT ON SCIENCE THREATENS YOUR HEALTH (OXFORD UNIVERSITY PRESS) (2008).
[22] Wagner, *Filter Failure, supra* note 19, *at* 1419.

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agenda-setting process. EPA should analyze whether certain communities are disproportionately affected by chemicals for which there is no IRIS information and strive to prioritize these assessments as well.

IRIS should push the regulatory agencies forward. It should also screen the epidemiology literature for candidate substances and provide information that prods the program offices to act under statutory authority. The relationship between the program offices and IRIS should be symbiotic and reinforcing.

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Appendix: Additional Tables of Chemicals Indicated by Program Offices Not Listed in IRIS

Table A1: Substances identified by CPR as CAA, SDWA, or Superfund data gaps that are being assessed by IRIS staff
Chemical
Arochlors (polychlorinated biphenyls)[1,2]
Cadmium[1]
Carbonyl sulfide[1]
Chloroform[1]
Cobalt[2,3]
1,2-Dichloroethane[1]
1,4-Dioxane[1]
Ethylene oxide[1,3]
Formaldehyde[1]
Methanol[1]
Methyl *tert*-butyl ether[3]
Methylene chloride[1]
Nickel[2]
Polycyclic aromatic hydrocarbons[2]
2,3,7,8-Tetrachlorodibenzo-p-dioxin[1,2]
Tetrachloroethylene[1]
Trichloroethylene[1]
[1]Air pollutants; [2]Superfund pollutants; [3]Drinking water contaminants

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Table A2: Hazardous Air Pollutants with Insufficient IRIS Information in Proposed or Mandated Residual Risk Rules	
Chemical	
Benzyl chloride	Hexachlorobenzene
Bis(chloromethyl) ether	Hexachloroethane
Bromoform	Hydrogen fluoride
Cadmium compounds	Isophorone
Carbonyl sulfide	Lead compounds
Chlorine	Lindane
Chlorobenzene	Mercury compounds
Chloroform	Methanol
Chloromethyl methyl ether	Methyl iodide
Cyanide compounds	Methyl isothiocyanate
2,4-D	N,N-Dimethylaniline
Dibenzofuran	Nickel compounds
1,2-Dichloroethane	o-Toluidine
Dichloromethane	Pentachloronitrobenzene
Diethyl sulfate	Phenol
Dimethyl carbamoyl chloride	Selenium
2,4-Dinitrophenol	Styrene oxide
2,4-Dinitrotoluene	1,1,2,2-Tetrachloroethane
1,4-Dioxane	Tetrachloroethylene
Dioxin and dioxin-like compounds	1,2,4-Trichlorobenzene
Ethyl acrylate	Trichloroethylene
Ethylene oxide	2,4,5-Trichlorophenol
Formaldehyde	2,4,6-Trichlorophenol

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Table A3: Hazardous Air Pollutants with Insufficient IRIS Information in the Hazardous Organic NESHAP
Chemical
Anthraquinone
Bromonaphthalene
Chloronaphthalene
Chrystene
Fluoranthene
Alpha-Naphthalene sulfonic acid
Beta-Naphthalene sulfonic acid
Alpha-Naphthol
Beta-Naphthol
Naphthol sulfonic acid
1-Naphthylamine
2-Naphthylamine
1,4-Naphthylamine sulfonic acid
1,2-Naphthylamine sulfonic acid
1-Nitronaphthalene
Tetrahydronaphthalene

These chemicals are not listed in the Clean Air Act Amendments of 1990 with the other HAPs profiled in this paper, but they were regulated by EPA under the Hazardous Organic NESHAP. We have included them because there is also insufficient IRIS information on these chemicals.

Table A4: ATSDR Priority Chemicals Listed for more than 10 years not in IRIS[23]	
Chemical	*ATSDR points*[24]
Aroclor 1240	888.11
Radon-220	804.54
Tributyltin	802.61
Neptunium-237	802.13
Iodine-129	801.64
Gamma-chlordene	702.59
Americium	701.62
Carbon Monoxide	684.49
Chromium trioxide	610.85
Benzopyrene	603.00
Actinium-227	602.57
Ethoprop	602.13
Alpha-chlordene	601.94
Calcium arsenate	601.48
Hydrogen fluoride	588.03
Pentaerythritol tetranitrate	545.59
Carbazole	534.52

[23] ATSDR, CERCLA PRIORITY LIST, *supra* note 11.

[24] Points are assigned by ATSDR is based on an algorithm that utilizes the following three components: frequency of occurrence at NPL sites, toxicity, and potential for human exposure to the substances found at NPL sites. *See* ATSDR, WHAT IS THE CERCLA LIST, *supra* note 13.

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Table A5: Water Contaminants Tracked under Unregulated Contaminant Monitoring, not in the CCL lists, not in IRIS
Chemical
2,2',4,4',5,5'-Hexabromobiphenyl
2,2,4,4',6-Pentabromodiphenyl ether
Dacthal di-acid degradate
Dacthal mono-acid degradate
Lead-210
Metolachlor ethane sulfonic acid
Metolachlor oxanilic acid
Polonium-210
Terbufos sulfone

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About the Center for Progressive Reform

Founded in 2002, the Center for Progressive Reform is a 501(c)(3) nonprofit research and educational organization comprising a network of scholars across the nation dedicated to protecting health, safety, and the environment through analysis and commentary. CPR believes sensible safeguards in these areas serve important shared values, including doing the best we can to prevent harm to people and the environment, distributing environmental harms and benefits fairly, and protecting the earth for future generations. CPR rejects the view that the economic efficiency of private markets should be the only value used to guide government action. Rather, CPR supports thoughtful government action and reform to advance the well-being of human life and the environment. Additionally, CPR believes people play a crucial role in ensuring both private and public sector decisions that result in improved protection of consumers, public health and safety, and the environment. Accordingly, CPR supports ready public access to the courts, enhanced public participation, and improved public access to information. The Center for Progressive Reform is grateful to the The John Merck Fund and the Bauman Foundation for funding this white paper. CPR also thanks the Public Welfare Foundation and the Deer Creek Foundation for their generous support of CPR's work on regulatory issues in general.

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UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON D.C. 20460

OFFICE OF THE ADMINISTRATOR
SCIENCE ADVISORY BOARD

The Honorable Lisa P. Jackson
Administrator
U.S. Environmental Protection Agency
1200 Pennsylvania Avenue, N.W.
Washington, DC 20460

Subject: Review Comments on EPA's Responsiveness to SAB 2007 Recommendations for the Revision of Cancer Assessment of Inorganic Arsenic

Dear Administrator Jackson:

The Science Advisory Board (SAB) received a request from the Office of Research and Development's National Center for Environmental Assessment to evaluate and comment on EPA's implementation of the SAB 2007 recommendations regarding the revision of the cancer assessment of inorganic arsenic. In response, a work group of the chartered SAB was convened to review the agency's document entitled, "*Toxicological Review of Inorganic Arsenic: In Support of the Summary Information on the Integrated Risk Information System (IRIS),*" (EPA/635/R-10/001), focusing on three areas: evaluation of epidemiological literature, dose-response modeling approaches, and the sensitivity analysis of the exposure assumptions used in the assessment. The SAB was not asked to conduct a full peer review of the assessment, including EPA's calculation of the cancer unit risk estimate. This report has been approved by the chartered SAB.

The SAB commends the agency on its efforts to be responsive to our previous recommendations. In keeping with SAB practice, public comments were considered by the SAB during the development of this report. The SAB has made a number of recommendations to improve the clarity and transparency of the 2010 draft assessment and to strengthen the scientific basis of EPA's findings and conclusions. Key recommendations are highlighted below.

In 2007, the SAB recommended the use of the epidemiologic data on the Taiwanese population for estimating bladder and lung cancer risk in humans from exposure to inorganic arsenic. The SAB also suggested that the agency consider other epidemiologic studies from the United States and other countries, utilizing a uniform set of evaluative criteria. On the basis of available data, the Taiwanese data set remains the most appropriate data set for determining the

cancer risk from exposure to inorganic arsenic. EPA's 2010 draft assessment presents a comprehensive overview of the epidemiological literature on arsenic carcinogenicity up to 2007; however, it needs to state more clearly the set of criteria that EPA used in evaluating and presenting the studies. Where possible, the summaries of the epidemiology studies should include a quantitative or qualitative presentation of the relative risk point estimates and the associated confidence intervals. Additionally, EPA should consider including an addendum or appendix describing major epidemiology studies that were published since 2007 and that could substantially impact the calculated cancer unit risk estimate.

In 2007, the SAB noted that there was a possibility of a nonlinear dose-response at low exposures to arsenic, but due to the lack of a complete understanding of the mode-of-action by which inorganic arsenic causes cancer in humans, the choice of a specific nonlinear model could not be justified. The SAB supports the agency's choice of using a default linear approach given the complexity of the mode-of-action of arsenic. Although extensive new research has been done in this area, there is not enough information in the literature to fully define the multiple modes-of-action for arsenic carcinogenicity.

The SAB, in 2007, also recommended that EPA consider using alternative dose-response models and perform a sensitivity analysis of the Taiwanese data with different exposure metrics. EPA's 2010 draft assessment uses a default linear low-dose extrapolation and evaluates the differences between a linear model and three non-linear models: quadratic, quadratic exponential and linear exponential. The SAB finds that, while the sensitivity analysis did respond to the 2007 recommendation, a more detailed description of the data sets used in the risk model is needed. Providing the distribution of variability of arsenic concentrations in well water and the data and parameters used in the modeling would help to make EPA's document more transparent. The SAB notes that, while EPA's choice of a linear approach is consistent with EPA's risk assessment default procedures, it has produced a calculated upper-bound cancer risk estimate for arsenic that is of significant public health concern. The SAB suggests that EPA discuss, possibly in other EPA complete risk assessment documents, how the estimated risks for arsenic should be interpreted in light of current estimated bladder and lung cancer incidence for the U.S. population.

In 2007, the SAB recommended that the agency conduct sensitivity analyses to determine the potential impact of different choices of exposure assumptions (both water and non-water consumption) for estimating arsenic cancer potency. The SAB finds that the agency was partially responsive to the previous recommendations. The SAB recommends that the agency revise its assessment to provide a more detailed and transparent explanation of the scientific rationale for its choice and use of alternative exposure assumptions. The SAB has also recommended ways to enhance the rigor and transparency of the sensitivity analysis for the exposure assessment through further documentation, explanation and analyses.

The SAB appreciates the opportunity to provide advice on EPA's inorganic arsenic cancer assessment. We look forward to the upcoming review of the IRIS assessment of non-cancer effects from arsenic exposure. The SAB underscores the importance of developing

integrated, interdisciplinary IRIS assessments and is amenable to conducting a future review of a synthesized assessment of arsenic health effects, as needed.

Sincerely,

/signed/

Dr. Deborah L. Swackhamer, Chair
EPA Science Advisory Board

/signed/

Dr. Elaine Faustman, Chair
SAB Arsenic Cancer Workgroup

NOTICE

This report has been written as part of the activities of the EPA Science Advisory Board, a public advisory committee providing extramural scientific information and advice to the Administrator and other officials of the Environmental Protection Agency. The Board is structured to provide balanced, expert assessment of scientific matters related to problems facing the Agency. This report has not been reviewed for approval by the Agency and, hence, the contents of this report do not necessarily represent the views and policies of the Environmental Protection Agency, nor of other agencies in the Executive Branch of the Federal government, nor does mention of trade names or commercial products constitute a recommendation for use. Reports of the EPA Science Advisory Board are posted on the EPA Web site at: http://www.epa.gov/sab.

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EXECUTIVE SUMMARY

Various committees have evaluated the assessment of cancer risk associated with exposure to inorganic arsenic. They include two National Research Council (NRC) committees (1999, 2001) and the EPA Science Advisory Board (SAB) in 2007. In 2010, EPA's National Center of Environment Assessment (NCEA) within the Office of Research and Development (ORD) requested the SAB evaluate and comment on the agency's implementation of the SAB recommendations in 2007 regarding EPA's revision of the cancer assessment of inorganic arsenic. In response, a workgroup of the chartered Board reviewed EPA's draft document entitled, "*Toxicological Review of Inorganic Arsenic: In Support of the Summary Information on the Integrated Risk Information System (IRIS)*," (EPA/635/R-10/001) and was asked to comment on three areas: evaluation of epidemiological literature; dose-response modeling approaches; and the sensitivity analysis of the exposure assumptions used in the risk assessment. The SAB was not asked to conduct a full peer review of the assessment, including EPA's calculation of the cancer risk estimate. A summary of the SAB responses to EPA's charge questions follows with further details included in the body of the report.

Evaluation of epidemiological data

The NRC in 1999 and 2001 concluded that ecological studies from the arsenic endemic area of Taiwan provide the best available empirical human data and are appropriate for use in dose-response assessment of arsenic in drinking water. In 2007, the SAB also supported the use of the epidemiologic data on the Taiwanese population for estimating human cancer risk for inorganic arsenic, especially to identify the potential range of responses of human populations.

The SAB agrees with these previous findings and the draft 2010 assessment that, based on the current data, the Taiwanese data set remains the most appropriate data set for determining the population risk of cancer from exposure to inorganic arsenic. The SAB also notes that the EPA's draft 2010 assessment includes a comprehensive listing of the epidemiological literature on arsenic and cancer up to 2007; however, the set of criteria that were used in evaluating the studies needs to be better presented. The SAB recommends that, where possible, the summaries of the epidemiology studies should include a quantitative or qualitative presentation of the relative risk point estimates for a specific exposure comparison and the associated confidence intervals. Furthermore, the SAB suggests that EPA consider including an addendum or appendix describing major epidemiology studies published since 2007 that could substantially impact the calculated cancer risk estimate.

Mode-of-action and sensitivity analysis of dose-response modeling

The NRC in 1999 and 2001 concluded that the available mode-of-action data on arsenic did not provide a biological basis for using either a linear or nonlinear extrapolation. In 2007, the SAB concluded that inorganic arsenic has the potential for a highly complex mode-of-action and until more was learned about the complex pharmacokinetic and pharmacodynamic properties of

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inorganic arsenic and its metabolites, there was insufficient justification for the choice of a specific nonlinear form of the dose-response relationship.

The SAB concludes that there are multiple potential mechanisms for arsenic carcinogenicity and potential target tissues. The SAB notes that although a large amount of research is available on arsenic's mode-of-action, the exact nature of the carcinogenic action of arsenic is not yet clear. Therefore, there is not enough information in the literature to define a mode-of-action for all of the relevant cancer endpoints for this assessment. The SAB recommends that this complexity and limited understanding of the mode-of-action of arsenic should be openly acknowledged in the 2010 draft assessment.

In 2007, the SAB recommended that EPA consider using alternative dose-response models and perform a sensitivity analysis of the Taiwanese data with different exposure metrics, with the subgroup of villages with more than one well measurement and using a multiplicative model that includes a quadratic term for dose. The SAB finds that the sensitivity analysis of dose-response modeling presented in the 2010 draft assessment was responsive to the SAB previous recommendations. The SAB agrees with the conclusion that none of the alternative models (i.e., quadratic, quadratic exponential and linear exponential) evaluated by EPA materially changed the estimated risk levels versus use of a linear model. EPA also evaluated whether the models were inordinately affected by the high end of the dose-response curve and found that they were not. However, the SAB believes that more transparency and a better scientific rationale for the agency's selection process are needed. To improve the clarity and transparency of the draft assessment, a number of aspects of the sensitivity analysis should be described in greater detail. They include the need for a more detailed description of the Taiwanese data sets used in developing the risk model; a better description of the distribution of well water arsenic concentrations across and within the 42 exposed villages; and a further explanation of the sensitivity displayed for female bladder cancer risks. The SAB notes that, while EPA's choice of a linear approach is consistent with EPA's risk assessment procedures, it has produced a calculated upper-bound cancer risk estimate for arsenic that is of significant public health concern. The SAB suggests that EPA discuss, possibly in other EPA complete risk assessment documents, how the estimated risks for arsenic should be interpreted in light of current estimated bladder and lung cancer incidence for the U.S. population.

Exposure assessment and sensitivity analysis

The 1999 NRC report noted that the assessment of arsenic exposure via drinking water is often based on the measurements of arsenic concentrations in drinking water and assumptions regarding the amount of water consumed. The 2001 NRC report added that the method used to characterize arsenic dose in a study is a source of uncertainty in arsenic dose-response assessment. Furthermore, the NRC report noted that the choice of the dose measurement affects the interpretation of an epidemiological study and the choice of the dose-response model. The 2007 SAB agreed that water consumption (via drinking water, in beverages, or in cooking water) assumptions could have an impact on the assessment of arsenic's risk. However, the 2007 SAB did not recommend specific values for EPA to use in evaluating dose-response in the Taiwanese study nor for levels of exposure in the U.S. population risk estimates. It instead recommended

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that uncertainty in exposure parameters be evaluated for both the Taiwanese study population and the U.S. populations through sensitivity analyses. The 2007 SAB recommended that EPA evaluate the drinking water consumption rate assumptions used with regard to highly exposed and sensitive subpopulations. Additionally, the NRC (2001) recommended that EPA consider the background dietary intake of inorganic arsenic and incorporate the adjustment values. The 2007 SAB also concluded that arsenic levels in food are important considerations for EPA's assessment of lung and bladder cancer risk associated with exposures to arsenic in drinking water. The 2007 SAB stated that a range of total arsenic food intake values should be included in the sensitivity analyses.

The SAB finds EPA's revisions to the IRIS assessment to be partially responsive to SAB's 2007 recommendations regarding the exposure assumptions. The SAB provides two primary general suggestions for improving the responsiveness of the assessment; they include, making more transparent the scientific basis of the exposure assumptions used; and enhancing the rigor and transparency of the sensitivity analysis. The basic approach to the sensitivity analysis is adequate for meeting the minimum requirements for the intended purpose, and is responsive to the SAB recommendation in that the impact of choice of assumptions is shown in terms of specific cancer risks (lung and bladder, males and females). There are sufficient data to support development of variability and/or uncertainty distributions for some inputs, such as drinking water consumption rates in the United States, but the data are not available to assign corresponding distributions for the Taiwanese populations.

The SAB notes that much of the documentation addressing the scientific basis of the exposure assumptions is available through separate documents (e.g. EPA Issues Paper, 2005d) that, if incorporated within the agency's draft IRIS assessment, will help address the SAB's concerns. The SAB recommends that relevant information from these documents be integrated within the current document as appropriate with the goal of enhancing transparency and scientific credibility. The SAB has provided specific suggestions, within the body of the report, for making the scientific basis of the exposure assumptions used more transparent and for enhancing the rigor, and transparency, of the sensitivity analyses.

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BACKGROUND

Arsenic is a naturally occurring element that is found throughout the environment. Exposure to inorganic arsenic can result in different health outcomes depending upon the route of exposure. Arsenic compounds are used as a mordant in the textile industry, for preserving hides, as medicinals, pesticides, pigments, and wood preservatives. EPA's health effects assessment for inorganic arsenic was first made available on the Integrated Risk Information System (IRIS) database in 1988. Various committees have reviewed aspects of the EPA's revised assessment of cancer risk associated with exposure to inorganic arsenic. They include two National Research Council (NRC) committees (1999, 2001) that concluded that the cancer risk for inorganic arsenic should be based on internal cancers (lung and bladder) instead of skin cancers. In 2005, the SAB was asked to review several EPA documents including:

- Office of Pesticide Programs' (OPP) *Draft Science Issue Paper: Mode-of-action for Cacodylic Acid (Dimethylarsinic Acid) and Recommendations for Dose Response Extrapolation* (U.S. EPA OPP, 2005a)
- Office of Research and Development (ORD) Issue Paper *Cancer Risk Assessment for Organic Arsenical Herbicides: Comments on Mode of Action, Human Relevance and Implications for Quantitative Dose-Response Assessment* (Appendix E of U.S. EPA OPP, 2005, USEPA ORD, 2005b).
- Office of Water's (OW) Draft *Toxicologic Review of Inorganic Arsenic* (U.S. EPA OW, 2005c).

At that time, the SAB convened a panel of experts to provide advice on the metabolism, mode of action, dose-response, and approaches to low-dose extrapolation of cancer risk for Dimethylarsinic Acid (DMA^{V}) and inorganic arsenic (iAs). The SAB review report (EPA-SAB-07-008) was issued in June 2007 and is available at http://yosemite.epa.gov/sab/sabproduct.nsf/02ad90b136fc21ef85256eba00436459/EADABBF40DED2A0885257308006741EF/$File/sab-07-008.pdf.

In 2010, ORD's National Center for Environmental Assessment (NCEA) requested the SAB evaluate and comment on EPA's implementation of SAB (2007) key recommendations in the 2010 draft assessment entitled, "*Toxicological Review of Inorganic Arsenic: In Support of the Summary Information on the Integrated Risk Information System (IRIS)*," (EPA/635/R-10/001). In response to this request, the SAB convened a workgroup of the chartered Board to comment on the agency's charge questions that focused on three areas: evaluation of epidemiological literature, dose-response modeling approaches, and the sensitivity analysis of the exposure assumptions used in the risk assessment. The SAB was not asked to conduct a full peer review of the assessment, including EPA's calculation of the cancer risk estimate. The SAB workgroup held a public face-to-face meeting, on April 6-7, 2010, to discuss and deliberate on its responses to EPA's charge questions. The chartered Board conducted a quality review of the work group's draft report (May 13, 2010) at a public teleconference on June 16, 2010 and a revised draft was again reviewed on November 22, 2010. The final SAB report incorporates the SAB quality review comments and public comments, both written and oral, which were received throughout the advisory process.

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RESPONSES TO EPA'S CHARGE QUESTIONS

Charge Question 1:

The SAB concluded that the Taiwanese data set (Wu 1989; Chen et al., 1988, 1992) remains the most appropriate data set to determine carcinogenic risk due to exposure to iAs. They recommended that EPA should evaluate other published epidemiology studies using a uniform set of criteria and document these findings in the assessment. They also stated that if one or more studies provide potential utility, comparisons should be provided in the assessment.

EPA agreed that the Taiwanese data were the best available for determining the carcinogenic risk due to exposure to iAs. In response to SAB's recommendation, an extensive review and evaluation of all available human studies for iAs using the criteria suggested by the SAB was performed by EPA and is summarized in Section 4.1 of the draft IRIS assessment and included in tabular format in Appendix B. EPA concluded in the 2010 draft IRIS assessment that there were no additional epidemiological studies that had comparable utility to the Taiwanese data set (Wu 1989; Chen et al., 1988, 1992).

Please comment on EPA's response to the recommendations and the conclusions of the SAB (2007) Arsenic panel regarding the evaluation of the epidemiological literature.

Response:

In 1999, the NRC concluded that ecological studies from the arsenic endemic area of Taiwan provide the best available empirical human data for assessing the risks of arsenic-induced cancer. The 2001 NRC report also concluded that the data from southwestern Taiwan remain appropriate for use in dose-response assessment of arsenic in drinking water. In 2007, the SAB supported the use of the epidemiologic data on the Taiwanese population for estimating human cancer risk for inorganic arsenic especially to identify the potential range of responses of human populations. The 2007 SAB urged the agency to consider other epidemiologic studies from the United States and other countries, utilizing a uniform set of evaluative criteria, as they develop their risk assessment. The 2007 SAB recommended consideration of the following additional factors when reviewing the studies:

1. Estimates of the level of exposure misclassification;
2. Temporal variability in assigning past arsenic levels from recent measurements;
3. The extent of reliance on imputed exposure levels;
4. The number of persons exposed at various estimated levels of waterborne arsenic;
5. Study response/participation rates;
6. Estimates of exposure variability;
7. Control selection methods in case-control studies; and
8. The resulting influence of these factors on the magnitude and statistical stability of risk estimates.

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The SAB concludes that EPA has been responsive to the 2007 SAB recommendations in evaluating the epidemiology studies published through 2007. The 2010 draft IRIS assessment presents a well organized and very comprehensive overview of the epidemiological literature on arsenic and cancer through 2007. The SAB recognizes that there are limitations that are inherent in the design of environmental epidemiological investigations, particularly regarding reconstruction of past exposure levels. EPA has described the limitations of each study in Section 4.1 of the draft IRIS assessment, and presented a summary of study strengths and limitations in the tables of Appendix B. The systematic review of the literature, however, needs to more clearly state the set of criteria that were used in evaluating the studies. Additional clarification and documentation on how various study design factors were considered and weighted in the evaluation are needed. In addition, there are aspects of studies that are discussed in Section 4.1 narrative that are not included in the summary table of Appendix B. The SAB recommends that the tables in Appendix B be reformatted to present the study summaries more clearly and in a more consistent format including adding any essential information from references into the text for clarity.

The SAB supports the 2007 SAB conclusion that the Taiwanese data set (Wu 1989; Chen et al., 1988, 1992) remains the most appropriate data set for determining the population risk of cancer to exposure to inorganic arsenic. The limitations of the Taiwanese studies are well presented, particularly regarding the ecologic study design, use of death certificates, and assumptions regarding lifetime individual arsenic exposure. The strengths of these studies include availability of community drinking water exposure levels, large populations and person-years of follow-up, and consideration of important potential confounders including socioeconomic status, lifestyle, dietary patterns, and medical care. The SAB acknowledges the concerns expressed regarding the limitations of the Taiwanese data set; however given the fundamental mission of EPA to protect public health, these well conducted and extensively reviewed studies remain the most appropriate critical studies.

The SAB received public comments that suggested when comparing the large number of epidemiological studies that demonstrate varying results the power calculations for the studies can provide important insights and should be taken into consideration. The power of an epidemiological study is the probability of detecting an association of a specified strength between exposure and disease if one exists. For example, in studies where statistical significance is not achieved, failure to identify an association may be a reflection of a limitation of the power of the study. The SAB, however, notes that while the relative power of various studies is important to convey, this should not be done by presenting only power calculations. Power calculations are useful in planning a study, but after the study is completed, the most informative presentation of epidemiologic findings that combines both the observed results and reflects the power of the study is the relative risk (RR) point estimates for a specified exposure comparison and the associated confidence intervals. Furthermore, systematic presentation of numbers of individuals in each exposure stratum provides the reader with a sense of relevant sample size within strata and the robustness of the exposure contrast. While a restricted range of exposure within a study population will limit estimation, it is also likely that studies carried out at a lower-level of exposure will be estimating an effect smaller than that at higher levels for a categorical comparison of higher-exposed to lower-exposed. For instance, the required sample size should be larger when a smaller range of exposures is observed (e.g., the U.S. studies), since the expected magnitude of the RR for low-level exposure is lower. The SAB also recognizes that many published arsenic studies may not present

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specific power calculations or RR and that a detailed quantitative comparison is difficult. Where possible, the summaries of the epidemiology studies should include a quantitative or qualitative presentation of the relative risk point estimates for a specific exposure comparison and the associated confidence intervals. This should be included both in the study descriptions in Section 4.1 and in the table of studies in Appendix B.

As noted by public comments, the SAB agrees that failure to control potential confounders or misclassification of study population exposure levels may bias study results. In the presentation of one of the critical epidemiology studies (Chen et al. 1992), the IRIS assessment (p.38) states, "a weakness of the study is the assumption that an individual's arsenic intake remained constant from birth to the end of the follow-up period; this flaw possibly led to the underestimation of risk." Other epidemiological studies also had similar issues. Indirect measures of individual exposure were used to estimate population exposure levels for all of the epidemiology studies. In Section 4.1, the narrative presenting the epidemiology studies should include a more detailed discussion of bias including literature citations addressing the potential for bias, both underestimating and overestimating of risk, due to confounders or limitations in exposure estimation. While the existence of bias can usually be proposed with some certainty, the key issue is whether the quantitative consequences of bias are of sufficient magnitude to be of concern. Methods are available for this purpose (see, for example: Lash, Fox, and Fink: *Applying Quantitative Bias Analysis to Epidemiological Data,* Springer, 2009). The SAB suggests that the IRIS assessment include a simple table that identifies potential biases (misclassification of exposure, misclassification of disease, omitting potential confounders, etc.) and the potential magnitude and direction of bias in inferences that are drawn from the study data. A simple summary could then relate these sources of bias to their impact in the data and methods used in the IRIS assessment.

The IRIS 2010 assessment includes an extensive review of published epidemiology studies up to and including the year 2007. The SAB recognizes that the assessment cannot be continually updated with every newly published paper and it is not the purpose of IRIS to provide real time summaries of advancing science. However, given the large amount of ongoing research on the health effects of arsenic, the SAB has concerns about the 2007 cutoff. In order to ascertain if new studies will impact the 2010 assessment, EPA should consider including an addendum or appendix describing major epidemiology studies published since 2007 (i.e., those studies that can influence the dose-response assessment due to large sample size or effect estimate that is substantially different from that estimated by Chen et al. (1988, 1992).

Charge Question 2:

The SAB noted the possibility of a nonlinear dose-response at low exposures, but due to uncertainty in the mode-of-action (including pharmacokinetics and dynamics) the use of a linear low dose extrapolation approach to determine the cancer risk for iAs was recommended using cancer incidence from the Taiwanese data set. In addition, the SAB stated that EPA should perform a sensitivity analysis for the variables in the cancer modeling with respect to the Taiwanese data set (i.e., exposure metrics, subgroup of villages with more than one well measurement, and a multiplicative model that includes a quadratic term for dose). The SAB

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concluded that overall, EPA had implemented the recommended modeling by NRC (2001). Also, the SAB made recommendations to perform a sensitivity analysis regarding the robustness of the model and alternative formulations.

Consistent with the SAB recommendations, EPA used a linear low-dose extrapolation approach and conducted a sensitivity analysis of nonlinear forms of the dose-response in the 2010 draft IRIS assessment. EPA also explored nonlinear forms of the dose-response from the Taiwanese data set (Wu 1989; Chen et al., 1988, 1992). Sensitivity analyses using alternative dose-response models produced potency estimates similar to the linear approach.

Please comment on EPA's response to the SAB's recommendations and conclusions regarding the approach to modeling inorganic arsenic cancer risks and the corresponding sensitivity analyses.

Response:

Mode-of-action and dose-response modeling

The 1999 NRC Committee concluded that the mechanism or mode-of-action by which inorganic arsenic causes toxicity, including cancer, is not well established. This conclusion was again supported by the NRC in 2001 which noted that although a large amount of research is available on arsenic's mode-of-action, the exact nature of the carcinogenic action of arsenic is not yet clear. Therefore, the 2001 NRC report concluded that the available mode-of-action data on arsenic did not provide a biological basis for using either a linear or nonlinear extrapolation.

In 2007, the SAB concluded that inorganic arsenic has the potential for a highly complex mode-of-action and until more is learned about the complex pharmacokinetic and pharmacodynamic properties of inorganic arsenic and its metabolites, there is not sufficient justification for the choice of a specific nonlinear form of the dose-response relationship. The NRC (2001) concluded that the most appropriate approach was to base risk assessments on a linear dose response model that includes the Southwestern Taiwan population as a comparison group.

The SAB agrees that there are multiple potential mechanisms for arsenic carcinogenicity and potential target tissues which make it very difficult to do a single risk assessment model. This complexity and limited understanding of the mode-of-action of arsenic should be openly acknowledged in the 2010 draft IRIS assessment. While there is an ever increasing literature on arsenic, there is not enough information in the literature to define a mode-of-action for all of the relevant cancer endpoints for this assessment. The SAB notes that it is a reasonable hypothesis that bladder cancer is the result of repeated cell injury, cell death and compensatory proliferation; but there is not enough specific data at this point to confirm the hypothesis, nor are there hypotheses to explain the role of arsenic in lung cancer. For these reasons, the SAB concurs with EPA's rationale for choosing a linear default approach for risk assessment.

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Sensitivity Analysis

The 2007 SAB recommended that EPA perform a sensitivity analysis of the Taiwanese data with different exposure metrics, with the subgroup of villages with more than one well measurement and using a multiplicative model that includes a quadratic term for dose. The SAB finds that the sensitivity analysis of dose-response modeling presented in the 2010 IRIS assessment was responsive to the previous 2007 SAB recommendations. Specifically, EPA was asked to evaluate a model using a quadratic term for dose. EPA evaluated the differences between a linear model and three non-linear models: quadratic, quadratic exponential and linear exponential. Results are described on p. 143, which concludes that "within the range of exposures covered by the epidemiological data, the alternative forms predict very similar risks." It would be very helpful if the results could be shown graphically, e.g., by showing the dose-response data and model dose-response curves for selected endpoints and age and gender classes. The SAB agrees with the conclusion that none of the alternative models materially changed the estimated risk levels versus use of a linear model. EPA also evaluated whether the models were inordinately affected by the high end of the dose-response curve. They were not. This was evaluated by running the models without the highest exposure group. EPA evaluated whether exclusion of a reference population influenced the dose-response curve. Results of this analysis (see Fig. 5-2) suggest that exclusion of the reference population did have an effect on risk estimates. EPA evaluated the pros and cons of including a comparison population in a 2005 issues paper (Issue Paper: Inorganic Arsenic Cancer Slope Factor, Final Draft, July 23, 2005). The SAB recommends that the rationale from the issue paper be included in the draft IRIS assessment, and the reference population described in greater detail. This will provide more transparency and strengthen the scientific rationale for the agency's selection process.

To improve the clarity and transparency of the draft IRIS assessment, there are a number of aspects of the sensitivity analysis that should be described in greater detail. They include:

- **More detailed description of underlying data.** The assessment would benefit from a more detailed description of the Taiwanese data sets used in developing the risk model. The data sets are briefly described in section 4.1.1 as part of the review of the Chen et al. 1988a, 1992 and Wu et al., 1989 studies, and key features are summarized in Table B-1. However, readers are required to piece together this information on their own in order to understand the basis for the risk modeling presented in section 5.3.

- **Variability of well water arsenic concentrations.** The distribution of well water arsenic concentrations across and within the 42 exposed villages is not adequately described. Only medians and ranges across the whole set of villages are presented in Table B-1. While the assessment mentions that the number ranged from 2 – 47 measurements, the variability of measurements both within and across wells within a given village is not provided. This information needs to be presented to assist in understanding the results of the sensitivity analysis the 2007 SAB requested. It would also be helpful to see a more quantitative characterization of how the 1974-1976 well water re-testing results differed from the results of tests conducted in 1962-1964, on which the risk modeling relied. Table B-1 indicates the results were "similar"; however, it is not clear how to interpret this.

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- **Upper and lower limits in water concentration.** EPA responded to SAB's request for sensitivity analysis or Monte Carlo analysis with respect to well water concentrations in the villages with more than a single measurement by re-estimating the model using minimum and maximum values of the concentrations for each village. Table 5-10 indicates the effect (in terms of estimated cancer incidence) is up to about a ± 30% change. Although EPA used upper and lower limits, rather than low and high percentile values or Monte Carlo analysis as SAB had suggested, the sensitivity analysis responds adequately to the recommendation. As noted above, however, more information on the variability in the underlying water concentration data is needed to substantiate the reported models and results.

- **Modeling data and parameters.** The SAB suggests that EPA publish the data and parameter tables used in its modeling analysis. As requested by the 2007 SAB report, this would strengthen the scientific credibility and transparency in the assessment.

- **Selection of a reference population.** EPA has tested the sensitivity of the risk model with respect to the choice of reference population (southwest Taiwan, all Taiwan, or no reference population) and to the value of non-water arsenic intake (i.e., in accordance with EPA's document, this refers to food intake) for both reference and exposed populations. Results indicate that the cancer incidence risks are fairly robust, with the exception of female bladder cancer risks. The sensitivity displayed for female bladder cancer risks seems to warrant further explanation – the result is described, but not explained, in the accompanying text (pp. 141-2). Additionally, EPA should examine whether any combinations of these parameter variations will affect the assessment– e.g., using different non-water intake values in combination with a different reference population.

The SAB notes that there is tremendous interest in the risk associated with consumption of water that is contaminated with inorganic arsenic and suggests that EPA discuss how their results should be interpreted in light of existing population-level data on bladder and lung cancer risk for exposure levels that are relevant for U.S. populations. The idea of providing a "reality check" on the estimated risk levels was discussed. The SAB recognizes that IRIS toxicological reviews are not intended to provide a complete risk assessment but rather a summary and synthesis of the toxicological evidence that supports risk assessment. Hence, an estimation of risk attributable to arsenic in drinking water in U.S. populations versus the observed incidence of cancer is not appropriate within the purview of this document. The SAB considers this as a difficult but important exercise and recognizes that this is probably better suited for inclusion in other risk assessment and characterization documents developed by the agency.

Charge Question 3:

The SAB did not recommend specific values for the exposure assumptions or parameters used in the cancer model. They did, however, recommend evaluating the impact on the cancer

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risk of using a range of values, assessing the variability, and conducting a sensitivity analysis for exposure parameters (e.g., water intake, background dietary exposure).

EPA evaluated the impact on the estimated cancer risk of using a range of exposure parameter values (e.g., water intake, background dietary exposure), assessed variability, and conducted a sensitivity analysis. After the completion of these analyses, values were chosen for exposure assumptions based upon the best available science taking into account the NRC (2001) recommendations.

Please comment on EPA's sensitivity analyses and choice of the exposure assumptions used in modeling cancer risk as recommended by the SAB (2007) Arsenic panel.

Response:

The 1999 NRC report noted that assessment of arsenic exposure via drinking water is often based on the measurements of arsenic concentrations in drinking water and assumptions regarding the amount of water consumed. Such data are estimates, the uncertainty of which will depend on the method used. The 2001 NRC report added that the method used to characterize arsenic dose in a study is a source of uncertainty in arsenic dose-response assessment. Furthermore, the NRC report noted that the choice of the dose measurement affects the interpretation of an epidemiological study and the choice of the dose-response model.

The 2007 SAB agreed that water consumption (via drinking as water, in beverages, or in cooking water) assumptions have a substantial impact on the assessment of arsenic's risk. However, the 2007 SAB did not recommend specific values for EPA to use in evaluating dose-response in the Taiwanese study nor for levels of exposure in the U.S. population risk estimates. It did recommend that uncertainty in this parameter be evaluated for both the Taiwanese study population and the U.S. populations at risk. The 2007 SAB recommended that EPA should:

1) Evaluate the impact of drinking water consumption rates associated with more highly exposed population groups with differing exposures and susceptibilities (e.g., children, pregnant women);
2) Incorporate variability parameters for individual water consumption into their analysis for dose-response in the Taiwanese population as they have done for the U.S. population;
3) Conduct sensitivity analyses of the impact of using a range of consumption values for the Taiwanese population;
4) Provide a better justification for assuming different consumption levels by gender or in the absence of such a justification, conduct additional sensitivity analyses to examine the impact of equalizing the gender-specific consumption level;
5) More fully articulate and document how different sources of water intake, as well as variability, are incorporated into the risk model (e.g. data for intake from beverages and cooking water).

The NRC (2001) recommended that EPA consider the background dietary intake of inorganic arsenic and incorporate the adjustment values of 0, 10, 30, and 50 μg per day into the

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cancer risk calculations. The 2007 SAB also agreed that arsenic levels in food are important considerations for EPA's assessment of lung and bladder cancer risk associated with exposures to arsenic in drinking water. However, the 2007 SAB once again did not recommend a specific value for EPA to use in its base risk assessment. It did recommend a range of values for consideration by EPA in its sensitivity analysis and the 2007 SAB offered suggestions to EPA for additional analytical steps to clarify the impact of food levels of arsenic on dose-response and exposure as it revises its risk estimates. The 2007 SAB recommended that EPA should:

1) Conduct sensitivity analyses using a range of total arsenic food intake values from at least 50 to 100 μg per day to perhaps as high as 200 μg per day to assess the impact of this range of dietary intakes on risk of lung and bladder cancer from exposure *via* drinking water in the Taiwan cohort;
2) Not assume that the control population has an intake value of zero arsenic from food;
3) Apply greater rigor in their discussions of data used in these assessments (e.g., sources, methodological and analytical issues, bioavailability); and
4) Give immediate research attention to the issue of arsenic bioavailability.

The SAB finds EPA's revisions to the IRIS assessment to be partially responsive to the 2007 SAB recommendations regarding the sensitivity analyses and choice of the exposure assumptions used in modeling cancer risk. The SAB provides two primary general suggestions for improving the responsiveness of the assessment. They include, making more transparent the scientific basis of the exposure assumptions used and enhancing the rigor and transparency of the sensitivity analysis.

The basic approach to the sensitivity analysis is adequate for meeting the minimum requirements for the intended purpose, and is responsive to the 2007 SAB recommendation in that the impact of choice of assumptions is shown in terms of specific cancer risks (lung and bladder, males and females). In evaluating the consequences of choices regarding modeling assumptions and intake values, the IRIS assessment states, "The agency felt that the currently available data were insufficient to support detailed probabilistic uncertainty and variability estimation." The SAB agrees with this conclusion. There are sufficient data to support development of variability and/or uncertainty distributions for some inputs, such as drinking water consumption rates in the United States, but the data are not available to assign corresponding distributions for the Taiwanese populations.

The SAB notes that much of the documentation addressing the scientific basis of the exposure assumptions was available through separate documents (e.g. EPA Issues Paper, 2005d) that if incorporated within the current assessment, will help address the SAB's concerns. The SAB recommends that relevant information from these documents be integrated within the current document as appropriate with the goal of enhancing transparency and scientific credibility.

The SAB is providing the following specific suggestions for making the scientific basis of the exposure assumptions used more transparent and enhancing the rigor and transparency of the sensitivity analysis.

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